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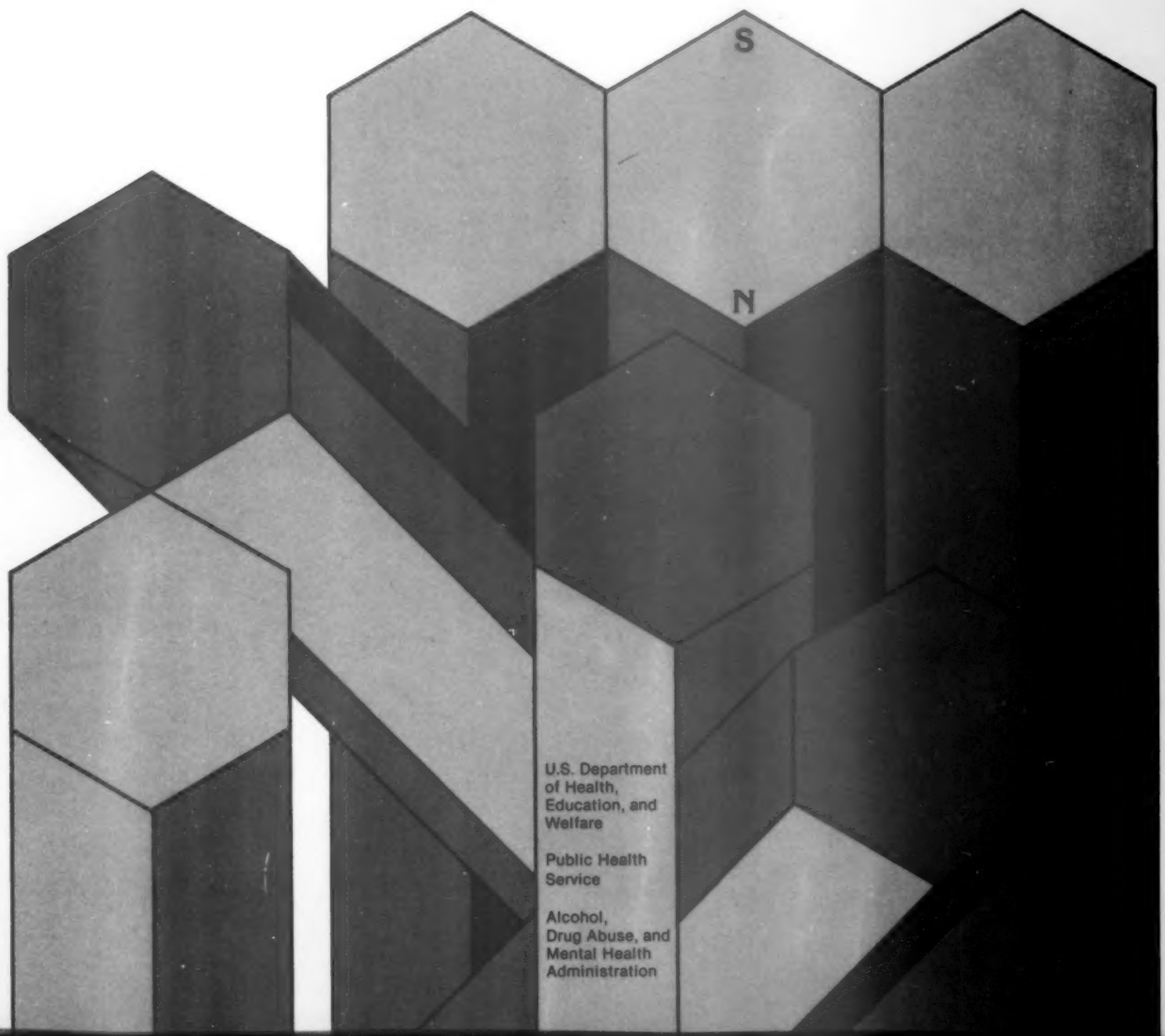

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Volume 16, Number 2 October 1978

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ABSTRACTS

PRECLINICAL PSYCOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

001000 Ager, I. R.; Danswan, G. W.; Harrison, D. R.; Kay, D. P.; Kennewell, P. D.; Taylor, J. B. Roussel Laboratories Ltd., Kingfisher Drive, Covingham, Swindon, Wiltshire, England **Central nervous system activity of a novel class of annelated 1,4-benzodiazepines, aminomethylene-2,4-dihydro-1H-imidazo(1,2-a)(1,4)benzodiazep in-1-ones.** Journal of Medicinal Chemistry. 20(8):1035-1041, 1977.

The synthesis and CNS activity of a novel class of annelated 1,4-benzodiazepines, the aminomethylene-2,4-dihydro-1H-imidazo(1,2-a)(1,4)benzodiazepines, are described. An investigation of the structure/activity relationships in the series derived from 8-chloro-2,4-dihydro-2-dimethylaminomethylene-6-phenyl-1H-imidazo(1,2-)(1,4)-benzodiazepin-1-one led to the synthesis of a group of compounds with potent minor tranquilizer activity. Pharmacologic studies in male rats for antiaggressive activity, anticonvulsant activities, potentiation of hexobarbital and chlorprothixene, the rotary drum test, and for acute toxicity are also reported. 11 references. (Author abstract modified)

001001 DeWald, Horace A.; Lobbestael, Sandra; Butler, Donald E. Chemistry Department, Warner-Lambert/Parke-Davis Pharmaceutical Research Division, Ann Arbor, MI 48106 **Pyrazolodiazepines. 2. 4-Aryl-1,3-dialkyl-6,8-dihydropyrazolo(3,4-e)(1,4)diazepin-7 (1H)-ones as antianxiety and anticonvulsant agents.** Journal of Medicinal Chemistry. 20(12):1562-1569, 1977.

A series of 4-aryl-1,3-dialkyl-6,8-dihydropyrazolo(3,4-e)(1,4)diazepin-7(1H)-ones was synthesized and screened for psychotropic activity. In animals, a number of these pyrazolodiazepinones had strong CNS effects similar to diazepam. One compound, 4-(2-fluorophenyl)-6,8-dihydro-1,3,8-trimethylpyrazolo (3,4-e)(1,4)diazepin-7(1H)-one (54), is being studied in the clinic as a component of a new animal anesthetic, Tilazol. 12 references. (Author abstract)

001002 Glennon, Richard A.; Gessner, Peter K. Dept. of Pharmaceutical Chemistry, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **The electronic and serotonin receptor binding affinity properties of n,n-dimethyltryptamine analogs.** Research Communications in Chemical Pathology and Pharmacology. 18(3):453-465, 1977.

The electronic and serotonin binding properties of a series of N,N-dimethyltryptamines and related analogs, for which binding affinity data are available, were examined using both a pi-electron and an all valence electron method. The results suggest that affinity is related to the ability of these compounds to donate electrons in a localized charge transfer manner from the 4-position of the indole nucleus. 20 references. (Author abstract)

001003 Hou, Joseph P. Squibb Institute for Medical Research, Georges Road, New Brunswick, NJ 08903 **The chemical constituents of ginseng plants.** Comparative Medicine East and West. 5(2):123-145, 1977.

The physiologically important chemical constituents of the dried roots and rhizomes of ginseng are discussed. These include ginseng saponins, ginseng oils and phytosterol, carbohydrates and sugars, organic acids, nitrogenous substances, amino acids and peptides, vitamins and minerals, and certain enzymes that have been isolated and characterized. Among these, ginseng saponins are proven to be the principal and most active constituents. Chemical research, therefore, has been focused on these saponins -- their extraction, purification, identification, isolation of aglycones, and biosynthesis. So far 13 saponins have been isolated and identified and these, which have been called ginsenosides or panaxosides, are triterpenes of dammarane and oleanane structures. Although American, Japanese, San-ch'i, Himalayan, and Siberian ginseng roots contain many saponins similar to those found in ginseng, the overall components in these ginseng species are quite different. The search for economical sources of ginseng saponins from nature and even chemical synthesis may likely become the active ginseng research of the future. 116 references. (Author abstract modified)

001004 Jiang, Jack B.; Hanson, Robert N.; Portoghese, Philip S.; Takemori, A. E. Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota, Minneapolis, MN 55455 **Stereochemical studies on medicinal agents. 23. Synthesis and biological evaluation of 6-amino derivatives of naloxone and naltrexone.** Journal of Medicinal Chemistry. 20(8):1100-1102, 1977.

Epimeric 6-amino derivatives of naloxone and naltrexone were synthesized and the configuration at the C-6 chiral center was determined from NMR studies. All of the derivatives possess narcotic antagonist activity in mice, with each of the 6 beta epimers having greater potency than the corresponding 6 alpha epimers. In vitro binding experiments indicate that the affinities of these epimers parallel their in vivo potencies. Slight antinociceptic properties were observed with three of the four compounds. The naloxone derivatives 3a and 3b appear to be attractive candidates for investigation as long acting narcotic antagonists in view of their fourfold greater duration of action relative to the other antagonists (1, 2, 4a, and 4b). 18 references. (Author abstract)

001005 Jonsson, John. Psychiatric Research Center, Ulleraker Hospital, University of Uppsala, 750 17 Uppsala, Sweden **Identification of metahydroxyamphetamine as a metabolite of amphetamine in the rat.** Research Communications in Chemical Pathology and Pharmacology. 18(2):189-199, 1977.

Identification is presented of a previously unknown metabolite of amphetamine. m-Hydroxyamphetamine (mOHA) was found as a metabolite of amphetamine in rat urine, liver perfusate, and bile. The identity was established with a gas chromatograph mass spectrometer (GC/MS) by its retention time, mass spectrum and selective ion monitoring of fragments representing both the side chain and the aromatic moiety. Furthermore, deuterium labeled amphetamine is used in order to circumvent the possibility of interference by substances with similar structure of endogenous or exogenous origin. The amount of mOHA was low, about 10% of the ring hydroxylation could be accounted for as metahydroxylation. 18 references. (Author abstract)

001006 Liuzzi, Antonia; Foppen, Fredrik H.; Saavedra, Juan M.; Levi-Montalcini, Rita; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Gas chromatographic-mass spectrometric assay of serotonin in rat superior cervical ganglia: effects of nerve growth factor and 6-hydroxydopamine.** Brain Research (Amsterdam). 133(2):354-357, 1977.

A highly specific gas chromatographic, mass spectrometric assay for serotonin was used to determine its levels in rat superior cervical ganglia and irises and the biosynthetic enzyme required for its formation was also measured. Results confirm the histological observations that treatment with NGF increases the serotonin contents of the superior cervical ganglia and the iris. The parallel increase in tryptophanhydroxylase of the ganglia suggests that serotonin is synthesized in the ganglia and that it is not the result of infiltration with platelets which contain serotonin but not tryptophanhydroxylase. It therefore appears that NGF stimulation of serotonin formation in the ganglia is due to action on cells that are present in the ganglia. The nature of the NGF stimulated serotonin containing cells remains unknown but it is unlikely that they are sympathetic neurons. 13 references. (Author abstract modified)

001007 Melrose, Joanne; Palfreyman, M. G.; Poyser, R. H.; Whiting, R. L. Beecham Pharmaceuticals, Research Division, Medicinal Research Centre, Coldharbour Road, Pinnacles, Harlow, Essex CM19 5AD, England **BRL 13776: a novel antihypertensive agent with interesting monoamine depleting properties.** British Journal of Pharmacology (London). 61(3):357-369, 1977.

To determine the effects of 7-n-pentyl-4-(1-(2-naphthylmethyl)--1,2,5,6-tetrahydro-4-pyridyl)-2,2- imethylchroman-5-01) (BRL-13776) an antihypertensive agent structurally related to the tetrahydrocannabinols, on brain catecholamine activity, a series of behavioral and physiological studies were undertaken in the rat and the cat. Data indicated that reduced blood pressure after BRL-13776 in rats is associated with catecholamine depletion occurred in all the peripheral tissues examined but in the brain was restricted to certain regions, these being the hindbrain on single dosing and the hindbrain, hypothalamus, and midbrain on repeated dosing. Catecholamine levels in the cerebral hemispheres were not affected by either single or repeated doses of BRL-13776. BRL-13776 caused some reduction of the 5-hydroxytryptamine content of the heart but not of whole brain or any brain region. Neither single doses nor repeated doses of BRL-13776 produced any significant behavioral effects in animals. BRL-13776 is a new type of agent to display both antihypertensive and monoamine depleting properties. The reduction of noradrenaline in certain brain regions may be a cause of the antihypertensive response but depletion in the periphery could contribute in a major or minor way. The differential action on noradrenaline in the brain together with the lack of effect on 5-hydroxytryptamine might also explain absence of behavioral effects. 39 references. (Author abstract modified)

001008 Misra, A. L.; Vadlamani, N. L.; Pontani, R. B. New York State Office of Drug Abuse Services, Testing and Research Laboratory, 80 Hanson Place, Brooklyn, NY 11217 **Evidence for a noncovalent intermolecular interaction of opiates with thiamine.** Research Communications in Chemical Pathology and Pharmacology. 18(3):581-584, 1977.

Ultraviolet spectroscopic evidence for a noncovalent intermolecular interaction of opiate agonists and antagonists with thiamine is presented. The spectra of these substances and their molecular complexes were measured in aqueous solution at ambient temperature of 25 degrees C. Opiate agonists and antagonists formed reversible molecular complexes with thiamine. The absorption maxima of these complexes were at wavelengths longer than those of the individual components and their intensities depended on the concentration and nature of the opiate component. The possible implications of such an interaction are briefly discussed. 12 references. (Author abstract modified)

001009 Nichols, David E.; Shulgin, Alexander T.; Dyer, Donald C. Dept. of Med., Chem. and Pharmacog., School of Pharm. and Pharm. Sci., Purdue University, West Lafayette, IN 47907 **Directional lipophilic character in a series of psychotomimetic phenethylamine derivatives.** Life Sciences (Oxford). 21(4):569-575, 1977.

Directional lipophilic character in a series of psychotomimetic phenethylamine derivatives was studied. Octanol/water partition coefficients (log P) were determined for a series of substituted psychotomimetic phenethylamine derivatives. A relationship was established between log P, steric bulk in the para position and the ability to stimulate serotonin receptors in an in vitro sheep umbilical preparation. It appears that log P values and in vitro activity in this preparation may be useful in predicting hallucinogenic potency in man. 13 references. (Author abstract modified)

001010 Portoghese, Philip S.; Hanson, Robert N.; Teland, Vasant G.; Winger, Jan L.; Takemori, A. E. Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota, Minneapolis, MN 55455 **3-hydroxy-17-aralkylmorphinans as potential opiate receptor-site-directed aklylating agents.** Journal of Medicinal Chemistry. 20(8):1020-1024, 1977.

In an effort to develop opiate receptor site directed alkylating agents, a series of 3-hydroxy-17-aralkylmorphinans containing reactive groups was synthesized and tested for analgesic and opiate antagonist activity. Many of the target compounds exhibited the characteristics of agonists and, among this group, some were found to be active blockers of morphine analgesia. One of the more potent antagonists (41) was investigated further and it was found that while its action is specifically associated with opiate receptors, 41 could not be classified either as a competitive or noncompetitive antagonist in the classical sense. The duration of antagonist action in vivo of 41 and its in vitro receptor binding characteristics suggest that covalent association with opiate receptors is not an important factor. 22 references. (Author abstract)

001011 Pummangura, S.; Nichols, D. E.; McLaughlin, J. L. Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmaceutical Sciences, Purdue Univ., West Lafayette, IN 47907 **Cactus alkaloids XXXIII: beta-phenethylamines from the Guatemalan cactus Pilosocereus maxonii.** Journal of Pharmaceutical Sciences. 66(10):1485-1487, 1977.

TLC analysis of extracts of Pilosocereus maxonii (Rose) Byles and Rowley which detected six identifiable alkaloids is presented. Preparative TLC aided in the crystallization of the hydrochlorides of N-methyl-3,4-dimethoxyphenethylamine, N-methyl-3-methoxytyramine, and N,N-dimethyl-3-methoxytyramine. Traces of 3,4-dimethoxyphenethylamine (TLC and mass spectrometry), tyramine (TLC), and N-methyltyramine (TLC) were identified. While all of these compounds were isolated and/or detected previously in other cactus species, this study is the first reported crystallization of N-methyl- and N,N-dimethyl-3-methoxytyramine from a natural source. 20 references. (Author abstract)

001012 Remy, David C.; Rittle, Kenneth E.; Hunt, Cecilia A.; Anderson, Paul S.; Engelhardt, Edward L.; Clineschmidt, Bradley V.; Scriabine, Alexander. Merck Sharp and Dohme Research Laboratories, West Point, PA 19486 **(+)- and (-)-3-Methoxycyproheptadine. A comparative evaluation of the antiserotonin, antihistaminic, anticholinergic, and orexigenic properties with cyproheptadine.** Journal of Medicinal Chemistry. 20(12):1681-1684, 1977.

The synthesis and resolution of (+ or -)-3-methoxycyproheptadine ((+ or-)-4) are described; and a comparative evaluation of the antiserotonin, antihistaminic, anticholinergic, and orexigenic properties with cyproheptadine is presented. As a peripheral serotonin antagonist, (+ or -)-4 was found to be one half as potent as cyproheptadine. The peripheral anticholinergic and antihistaminic activities as well as the orexigenic property of (+ or -)-4 are less than those of cypropheptadine. A further comparison of the enantiomers (+)-4 and (-)-4 shows that all of the anticholinergic activity of (+ or -)-4 resides solely in the dextrorotary enantiomer, (+)-4, while the antiserotonin activity, which is similar to that of 1b, resides in the levorotatory enantiomer, (-)-4. Antihistaminic and orexigenic activity also resides in (-)-4 but these properties are reduced compared to those of cyproheptadine. 7 references. (Author abstract modified)

001013 Repetto, M.; Lopez-Artiguez, M. Instituto Nacional de Toxicologia, Sevilla, Spain **Separation of cannabinoids.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):229, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, the development of a separative gas liquid chromatographic technique is reported. The technique was developed to make available isolated cannabic products for research purposes. A preparative gas chromatograph instrument provided with three 0.9m long SE-30 columns is used and pure CBN/; delta-THC and CBD are collected in different traps. (Journal abstract modified)

001014 Roseboom, H.; Perrin, J. H. Farmaceutisch Lab. Rijksuniversiteit Utrecht, Catharijnesingel 60, Utrecht, The Netherlands **Mechanism for phenothiazine oxidation.** Journal of Pharmaceutical Sciences. 66(10):1395-1398, 1977.

The mechanism of phenothiazine degradation was studied by following the degradation of 3,10′-diphenothiazine in ethanol/water mixtures as well as the electrochemical oxidation of phenothiazine. A mechanism, including the formation of an oxidized dimer and some polymers, is suggested. The experiment process is described in detail and the scheme and results are illustrated and fully discussed. 10 references. (Author abstract modified)

001015 Roseboom, H.; Perrin, J. H. Farmaceutisch Lab. Rijksuniversiteit Utrecht, Catharijnesingel 60, Utrecht, The Netherlands **Oxidation kinetics of phenothiazine and 10-methylphenothiazine in acidic medium.** Journal of Pharmaceutical Sciences. 66(10):1392-1395, 1977.

The rate of phenothiazine degradation in an acidic oxygen saturated medium was studied. 3H-Phenothiazine-3-one and phenothiazine 5-oxide are produced by parallel reactions, and 7-(10′-phenothiazinyl)-3H-phenothiazine-3-one is produced in a more complex manner. The overall phenothiazine degradation rate appears to be pH independent up to pH 7.0. The degradation kinetics of 10-methylphenothiazine were studied after isolation and identification of its degradation products, 10-methylphenothiazine 5-oxide and 3H-phenothiazine-3-one. The main degradation product is 10-methylphenothiazine 5-oxide; but at low pH values and high temperatures, more 3H-phenothiazine-3-one is formed. The degradation rate of 10-methylphenothiazine is pH independent up to pH 7. 17 references. (Author abstract)

001016 Vree, T. B. Department of Clinical Pharmacy, Radboudhospital, University of Nijmegen, Nijmegen, The Netherlands **Mass spectrometry of cannabinoids.** Journal of Pharmaceutical Sciences. 66(10):1444-1450, 1977.

The mechanism of fragmentation of cannabinoids to fragments m/e 314, 299, 271, 258, 246, 243, and 231 is given. Cannabidiol, cannabinodiol, cannabinol, delta6 and delta1-tetrahydrocannabinol, cannabichromene, cannabicyclol, derivatives with pentyl, propyl, and methyl side-chains, their methyl ethers, and cis-trans and ortho-para isomers were analyzed by GLC mass spectrometry using different energies for fragmentation during GLC elution. The following mechanism was distinguished: loss of a methyl radical, ring closure and rotation, McLafferty rearrangement, retro Diels-Alder, internal protonation, isomerization and internal bond formation, and one step fragmentation to m/e 231. 7 references. (Author abstract)

001017 Walser, Armin; Zenchoff, Gladys. Chemical Research Department, Hoffman-La Roche Inc., Nutley, NJ 07110 **Quinazolines and 1,4-benzodiazepines. 81. s-Triazolo(4,3-a)(1,4)benzodiazepines by oxidative cyclization of hydrazones.** Journal of Medicinal Chemistry. 20(12):1694-1697, 1977.

s-Triazolo(4,3-a)(1,4)benzodiazepines bearing various substituents in the 1 position were prepared by oxidative cyclization of the appropriate aldehyde hydrazones of 2-hydrazinobenzodiazepines. Diethyl azodicarboxylate and activated manganese dioxide were used as oxidizing agents. The new triazolo compounds were active in the CNS tests but none of them reached the potency of the known triazolobenzodiazepines. 9 references. (Author abstract)

001018 West, Leslie G.; McLaughlin, Jerry L. Dept. of Foods and Nutrition, School of Consumer & Family Sciences, Purdue University, West Lafayette, IN 47907 **Triterpenes from the button cactus, Epithelantha micromeris.** Journal of Natural Products. 40(5):499-504, 1977.

A study is reported of the toxicity to mice of ethanolic extracts (triterpenes) of the button cactus, epithelantha micromeris, a plant whose ritual ingestion by the Tarahumara Indians is known to have psychotropic effects. Acid hydrolysis of the toxic extracts permitted the isolation of six crystalline compounds. The known triterpenes oleanolic acid and methyl machaerinate and the common plant sterol, beta-sitosterol, were identified. The structures of two other isolated compounds, named epithelanthic acid and methyl epithelanthate, were postulated to be new delta9-(11)-12 oxo-oleanenes, and another trace compound was incompletely categorized as a triterpene lactone. 27 references. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

001019 Abbas, Rana; Willette, Robert E.; Edwards, J. Michael. School of Pharmacy, University of Connecticut, Storrs, CT 06268 **Piperidine derivatives: synthesis of potential analgesics in 3-substituted 4-phenylpiperidine series.** Journal of Pharmaceutical Sciences. 66(11):1583-1585, 1977.

The syntheses of 1-methyl-3-(3-hydroxy-3-phenylprophyl)-4-phenyl-4-piperidinol and 1-methyl-3-(3-hydroxy-3-phenylpropyl)-4-phenyl-4-propanoyloxypiperidin are described. Preliminary pharmacological testing in mice revealed that the compounds were inactive in the hot plate test and in the tail flick test but weakly active in the writhing test. 10 references. (Author abstract modified)

001020 Abdallah, Abdulmuniem H. Pharmaceutical R&D, Dow Chemical Company, Midland, MI 48640 **Preclinical**

evaluation of DITA (3′,4′-dichloro-2-(2-imidazolin-2-yl-thio)acetophenone hydrobromide): a new anorexigenic agent. Toxicology and Applied Pharmacology. 41(2):329-335, 1977.

A test of the anorexigenic activity of DITA (3′4′-dichloro-2-(2-imidazolin-2-yl-thio)acetophenone hydrobromide) in mice, rats, cats, and dogs showed it caused anorexia in all species tested. This compound, which possesses a novel chemical structure, produced increased motor activity in mice, but its effects on the cardiovascular system of anesthetized dogs were less marked than those of d-amphetamine. Repeated intragastric administration of DITA caused significant reduction of bodyweight in rats. In mice, DITA was found to have a more favorable therapeutic index than 3-amphetamine, and was similar to diethylpropion in action. 8 references. (Journal abstract modified)

001021 Anden, Nils-Erik; Johnels, Bo. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Effect of local application of apomorphine to the corpus striatum and to the nucleus accumbens on the reserpine-induced rigidity in rats.** Brain Research (Amsterdam). 133(2):386-389, 1977.

The importance of dopamine (DA) mechanisms in the neostriatum and in the nucleus accumbens for the muscle tone was investigated by giving local injections of apomorphine in these regions of reserpine treated rats. Apomorphine given into the corpus striatum caused a marked and dose dependent reduction of the reserpine induced rigidity lasting for about 1 hour. Systemic treatment with haloperidol 30 minutes prior to apomorphine completely inhibited the effect of apomorphine. Apomorphine given into the nucleus accumbens did not produce any clearcut change in the reserpine induced rigidity. The application of apomorphine to the corpus striatum caused intense stereotypies such as gnawing and licking. These effects were not seen after pretreatment with haloperidol or after injections into the nucleus accumbens. Apomorphine given into the nucleus accumbens resulted in a different type of hyperactivity such as movements of the extremities. It is suggested that the rigidity and the akinesia induced by reserpine in rats might be the result of a functional DA deficiency in the neostriatum and in the nucleus accumbens, respectively. 14 references.

001022 Archer, Giles A.; Kalish, Robert I.; Ning, Robert Y.; Sluboski, Barbara C.; Stempel, Arthur; Steppe, Thomas V.; Sternbach, Leo H. Chemical Research Department, Hoffman-LaRoche Inc., Nutley, NJ 07110 **Quinazolines and 1,4-benzodiazepines. 82. 5-pyrimidyl- and 5-pyrazinyl-benzodiazepines.** Journal of Medicinal Chemistry. 20(10):1312-1317, 1977.

Analogues of bromazepam (7-bromo-1,3-dihydro-5-(2-pyridyl)-2H-1,4-benzodiazepin-2-one,A), which is a clinically useful minor tranquilizer, were prepared by replacing the 2-pyridyl group at position 5 with 4-pyrimidyl(5), 2-pyrazinyl(8)2, 5-dimethylpyazin-3-yl(10), and 2-pyrimidyl (12) groups. Low to moderate CNS activities in both mice and cats were found for all the new compounds. For the screening procedures used, the 2-pyrimidyl substituted derivatives were found to be the most active new analogues although none of the activities exceeded those observed for bromazepam. 18 references. (Author abstract)

001023 Blanc, Marcel. no address **/Cataleptogenic properties of beta-endorphin./** Une nouvelle vedette: la beta-endorphine. Recherche (Paris). 8(74):86-87, 1977.

Endorphins, which are peptides capable of binding to morphine receptors, are discussed. It has been observed that beta-endorphin abolishes the reaction of the rat to tail pinch, and does this for a much longer period and at 1/100 the dose needed for met-enkephalin to produce this effect. Also, beta-endorphin induces a state of cataleptic muscular rigidity and total absence of spontaneous movement. A rat given beta-endorphin can be placed in an abnormal position and will maintain that position for 2 1/2 hours. Neither met-enkephalin, alpha-endorphin, gamma-endorphin, nor morphine produces this degree of catalepsy. Animals given these peptides intracerebrally develop violent muscular shaking 90 sec later, similar to the shaking of a wet dog or the withdrawal symptoms of a morphine dependent animal. Intracerebrally injected beta-endorphin is the only peptide which produces analgesia. All the peptides induce a CNS sedation, but beta-endorphin is the most powerful. Also, beta-endorphin binds to the morphine receptors more strongly and more durably than do the enkephalins.

001024 Dutta, A. S.; Gormley, J. J.; Hayward, C. F.; Morley, J. S.; Shaw, J. S.; Stacey, G. J.; Turnbull, M. T. Research Department, I.C.I. Limited, Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire, England **Enkephalin analogues eliciting analgesia after intravenous injection.** Life Sciences (Oxford). 21(4):559-562, 1977.

To clarify previous reports that enkephalin failed to cross the blood-brain barrier assays were made with i.v. administration. Extensive study of structure/activity relations in enkephalin like peptides led to identification of enkephalin analogs which are up to 70 times more potent than Leuenkephalin in vitro in the electrically stimulated guinea pig ileum preparation, and which are analgesic in the mouse hotplate test at doses as low as 5mg/kg following intravenous administration. Data are presented for 20 enkephalin analogs. 13 references. (Author abstract modified)

001025 Ebert, D. M.; Dren, A. T. Abbott Laboratories, North Chicago, IL 60064 **Intraocular pressure lowering properties of Abbott-43981, a cannabinoid-derived heterocyclic benzopyran with minimal CNS activities.** Pharmacologist. 19(2):230, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the pharmacological effects of Abbott-43981, a cannabinoid derived heterocyclic benzopyran, was reported. Topical or intravenous Abbott-43981 decreased intraocular pressure in rabbits but the drug was relatively inactive after intramuscular or oral administration. In contrast to other compounds derived from the cannabinoid nucleus, Abbott-43981 has minimal CNS activity as determined by: 1) a lack of hyperexcitability inducing properties in dogs after oral administration; 2) no effects on spontaneous motor activity and methamphetamine induced hyperactivity in rats after oral administration; and 3) no effects on DOPA elicited motor responses and footshock induced fighting in mice after oral administration. (Author abstract modified)

001026 Fries, David S.; Andrako, John; Hudgins, Patricia. Dept. of Pharmaceutical Chemistry, School of Pharmacy, Virginia Commonwealth University, Richmond, VA 23298 **Synthesis and preliminary pharmacological activity of aminoalkoxy isosteres of glycolate ester anticholinergics.** Journal of Medicinal Chemistry. 20(10):1250-1254, 1977.

A series of 2-(N-substituted amino)alkoxy-1,1-diphenylethanols was synthesized and evaluated in the rat for an-

ticholinergic activity. The compounds differ structurally from the glycolate ester type anticholinergic compounds by the bioisosteric substitution of a methylene group for the ester carbonyl moiety. The ethers which result from this change have increased lipophilicity compared to their ester isosteres. Compounds in the series have significant anticholinergic activity when tested on isolated rat jejunum or for their ability to inhibit perphenazine induced catatonia in rats. Structure/activity relationships of the compounds are discussed. 26 references. (Author abstract)

001027 Gold, M. S.; Redmond, D. E., Jr.; Donabedian, R. K. Dept. of Laboratory Medicine, Yale University, New Haven, CT 06510 **Animal prolactin evidence for antipsychotic activity of piperoxane.** Lancet (London). No. 8028:96-97, 1977.

In a letter to the editor, evidence in monkeys to suggest an antipsychotic effect for a new class of compounds represented by the alpha-adrenergic antagonist, piperoxane is presented. Six Macaca arctcides were given piperoxane or saline for 1 month. Piperoxane produced a significant rise in serum prolactin from a mean of 25ng/ml to 142ng/ml 15 minutes after drug infusion. The monkeys receiving piperoxane showed large increases in serum prolactin, while there were no significant changes in serum prolactin for the control animals. It is believed that piperoxane affects dopaminergic neurotransmission and has effects in animals similar to certain antipsychotics. It is suggested that piperoxane induced increases in serum prolactin may reflect the inhibition of dopaminergic impulse flow in the median eminence, either directly or through the large increase in noradrenergic activity and turnover, both mechanisms being different from the prolactin stimulating effect of known antipsychotics. 10 references.

001028 Hablitz, John J.; Wray, David V. Neurophysiology Department, Methodist Hospital, Baylor College of Medicine, Houston, TX 77030 **Cerebellar unit activity during generalized penicillin epilepsy in the awake cat.** Experimental Neurology. 56(1):189-199, 1977.

Single unit activity in the cerebellum of awake cats was recorded during generalized paroxysmal activity induced by intramuscular administration of penicillin. Subject animals (n=6) were surgically prepared with microelectrode implacement advanced through the dura. Cerebellar and neocortical brain electrical activity were monitored. Neocortical paroxysm appearances provoked changes in gross electrical activity of the cerebellum that were associated with altered neuronal activity. Along with the cerebellar paroxysms, Purkinje cells showed one of two types of activity: an increase in simple spike discharges associated with the surface negative phase of the paroxysm, or an excitatory inhibitory sequence. Normal firing patterns resumed quickly after cessation of the paroxysmal discharges. Results suggest that the cerebellum is a potential source of abnormal input of reticular (via fastigibulbar pathways) and thalamic (dentatothalamic) structures and may serve to increase or prolong paroxysmal activity when it is initiated. 32 references. (Journal abstract modified)

001029 Hahn, E. F.; Fishman, J.; Shiwaku, Y.; Foldes, F. F.; Nagashima, H.; Duncalf, D. Institute for Steroid Research, Rockefeller University, 1230 York Ave., New York, NY 10021 **The agonist and antagonist properties of N-allyl-enkephalins.** Research Communications in Chemical Pathology and Pharmacology. 18(1):1-9, 1977.

The agonist (ID 50) and antagonist (Ke) potencies of the newly synthesized N-allyl derivatives of Met5-enkephalin and Leu5-enkephalin were compared with those of their respective parent compounds on the myenteric plexus longitudinal muscle preparation of the guinea-pig ileum. N-allyl substitution of the amine nitrogen in the Met5-enkephalin significantly decreased both the ID 50 and the Ke. In contrast, similar substitution in Leu5-enkephalin did not sifnificantly alter the ID 50, but caused an almost tenfold increase in the Ke. The results suggest that substitution on the amine/nitrogen of Leu5-enkephalin rather than Met5-enkephalin is more likely to produce potent narcotic antagonists. 22 references. (Author abstract)

001030 Jacob, Peyton, III; Anderson, George, III; Meshul, Charles K.; Shulgin, Alexander T.; Castagnoli, Neal, Jr. Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, CA 94143 **Monomethylthio analogues of 1-(2,4,5-trimethoxyphenyl)-2-aminopropane.** Journal of Medicinal Chemistry. 20(10):1235-1239, 1977.

Regiospecific syntheses of the three monomethylthio analogues of 1-(2,4,5-trimethoxyphenyl)-2-aminopropane are described and their evaluation for potential psychotomimetic potency using the rabbit hyperthermia assay is presented. Enantiomeric compositions and time/concentration curves in rat brains were determined following intraperitoneal administration of each compound. The biological data are contrasted with the corresponding results obtained with the potent human psychotogen 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM). 25 references. (Author abstract)

001031 Jacquet, Yasuko F.; Klee, Werner A.; Rice, Kenner C.; Iijima, Ikuo; Minamikawa, Junichi. New York State Research Institute for Neurochemistry and Drug Addiction, Rockland Psychiatric Institute, Ward's Island, NY 10035 **Stereospecific and nonstereospecific effects of (+)- and (-)-morphine: evidence for a new class of receptors?** Science 198(4319):842-845, 1977.

Stereospecific and nonstereospecific effects of (+)-morphine and (-)-morphine were studied. Results indicate that the unnatural (+) enantiomer of morphine had minimal activity in three opiate assays in vitro: the rat brain homogenate binding assay, the electrically stimulated guinea pig ileum assay, and the inhibition of adenylate cyclase in neuroblastoma x glioma hybrid cell homogenates. When (+)-morphine was microinjected into the periaqueductal gray (a site known to mediate morphine analgesia) of drug naive rats, there was only minimal analgesia, but the hyperresponsivity usually observed after microinjection of (-)-morphine occurred. Also, when (+)-morphine was microinjected into the midbrain reticular formation of drug naive rats, rotation similar to that following microinjection of (-)-morphine occurred. These behaviors were not blocked by naloxone. Significantly, they typically occur in precipitated abstinence in morphine-dependent rats. These observations suggest that there are at least two classes of receptors, one stereospecific and blocked by naloxone and the other only weakly stereospecific and not blocked by naloxone, and that precipitated abstinence may be due in part to a selective blockade of receptors of the former class but not of the latter. 31 references. (Journal abstract modified)

001032 Kaplan, Bonnie J. Neuropsychology Laboratory, Veterans Administration Hospital, West Haven, CT 06516 **Phenobarbital and phenytoin effects on somatosensory evoked potentials and spontaneous EEG in normal cat brain.** Epilepsia. 18(3):397-403, 1977.

The results of a study in which chronic oral administration of phenobarbital and phenytoin was studied in chronically implanted cats are presented. The effects of two dosages were

analyzed with two physiological measures: somatosensory evoked potentials and power spectral analysis of the EEG. The results are interpreted as demonstrating: 1) minimal EEG and SEP modifications at the cerebral cortical level due to nontoxic dosages of phenobarbital and phenytoin; 2) a selective phenytoin effect on the dentatothalamic outflow of the cerebellum and on the dorsal hippocampus; and 3) a potential usefulness of peak frequency analysis as a measure of EEG response to anticonvulsant. 20 references.

001033 Kolb, Bryan; Whishaw, Ian Q. Department of Psychology, University of Lethbridge, Lethbridge, Alberta T1K 3M4, Canada **Effects of brain lesions and atropine on hippocampal and neocortical electroencephalograms in the rat.** Experimental Neurology. 56(1):1-22, 1977.

The relation between neocortical and hippocampal electroencephalogram (EEG) activity and behavior was studied in rats with forebrain and brainstem lesions. Subject animals (n=134) were lesioned and electrodes were implanted in the hippocampus and in the sensorimotor neocortex of each hemisphere. The following tests and observations were performed: 1) EEG activity for 100 day duration; 2) behavioral observations; 3) wheel running; 4) swimming; 5) sensory and behavioral tests; 6) atropine treatments; and 7) brain dissection at conclusion of experiment. Atropine sensitive neocortical low voltage, fast activity (LVFA) recorded during immobility could be transiently abolised by lateral hypothalamic lesions. Atropine sensitive hippocampal rhythmical slow activity (RSA) was produced by all brainstem lesions and became the dominant hippocampal EEG pattern in the alert immobile rat after medial pons lesions. Atropine resistant LVFA and RSA normally associated with movement could be transiently abolished by lateral hypothalamic and orbital frontal lesions. In addition, lateral hypothalamic lesions produced an acute reduction in RSA frequency, during walking and swimming, of 1 to 4 HZ which lasted 1 to 15 days, and a chronic reduction of about 1 Hz. The results support the suggestion that there are two types of LVFA and RSA, one of which is cholinergic, and further suggest that forebrain EEG activity may be related to the higher order control movement activation. 44 references. (Journal abstract modified)

001034 Lee, Cheuk-Man; Michaels, Raymond J.; Zaugg, Harold E.; Dren, Anthony T.; Plotnikoff, Nicolas P.; Young, Patrick R. Division of Pharmacology and Medical Chemistry, Abbott Laboratories, North Chicago, IL 60064 **Cannabinoids. Synthesis and central nervous system activity of 8-substituted 10-hydroxy-5,5-dimethyl-5H-(1)benzopyrano(4,3-c)pyridine and derivatives.** Journal of Medicinal Chemistry. 20(11):1508-1511, 1977.

The pharmacological activity of several nitrogen analogues of the tetrahydrocannabinols are studied as a continuation of synthetic work in the cannabinoid field. 8-(1,2-Dimethylheptyl) and 8-(5-(4-fluorophenyl)-2-pentyl)-10-hydroxy-5,5-dimethyl-5H-(1)benzopyr no(4,3-c)pyridines (2a and 2b), their phenolic ester and ether derivatives, and their N-oxides are synthesized and evaluated in various central nervous system pharmacological tests in animals. Compound 2a is generally the most active in this series with 2b being only slightly less active. It is suggested that the potency of nitrogen containing heterocyclic cannabinoids can be maintained or even increased slightly by aromatizing the hydroheteroaromatic ring to a pyridine ring. 6 references.

001035 Nielsen, I. Moller; Boeck, V.; Christensen, A. V.; Danneskiold-Samsoe, P.; Hyttel, J.; Langeland, J.; Pedersen, V.; Svendsen, O. Department of Pharmacology and Toxicology, H. Lundeck & Co. A/S, Ottiliavej 7-9, DK-2500 Valby, Denmark **The pharmacology of a new potent, long acting neuroleptic, piflutixol.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(4):369-383, 1977.

To elucidate the psychopharmacology of 6-fluoro-9-(3-(4-(2-hydroxyethyl)piperidino)-propylidine)-2-trifluorom thyl-thioxanthene (piflutixol), a series of behavioral studies were undertaken in rats, mice, dogs, and rabbits. Results indicate that piflutixol has pronounced neuroleptic properties. It is a very potent inhibitor of methylphenidate induced stereotypics in mice, amphetamine and apomophine induced stereotypics in rats, and apomorphine induced stereotypies and vomiting in dogs. Furthermore piflutixol causes cataleptic reaction in small doses and inhibits conditioned avoidance reaction in rats. The compound is equally potent orally and parenterally and has a prolonged effect. Piflutixol has up to the present proved to be the most potent inhibitor of dopamine stimulated adenylate cyclase in rat striatum in vitro. Piflutixol has a strong sedative effect (inhibition of spontaneous motor activity, induction of ptosis and potentiation of barbiturate anesthesia) and in addition inhibits reticular arousal reaction in very low doses. Thus piflutixol constitutes a unique combination of potent antistereotyped activity with potent sedative effects. This means that piflutixol may prove to be a low dose basic neuroleptic with long duration of action. 14 references. (Author abstract modified)

001036 Roemer, Dietmar; Buescher, Heinz H.; Hill, Ronald C.: Pless, Janos; Bauer, Wilfried. Biological and Medical Research Division, Sandoz Ltd., CH-4002 Basel, Switzerland **A synthetic enkephalin analogue with prolonged parenteral and oral analgesic activity.** Nature (London). No. 5620:547-549, 1977.

A number of pharmacological properties of synthetic pentapeptides structurally related to met-enkephalin are reported. Oxidation to the sulphoxide (D-Ala2,Met(0)5-ol) and N-methylation of the phenylalanine residue gave compound FK 33-824 (referred to as 33-824). The long-lasting analgesic effect of 33-824 is noted. The ready availability and stability of 33-824 are seen as making it valuable for further studies of the mode of action of opioid peptides. 33 references.

001037 Saner, A.; Pletscher, A. Research Division, F. Hoffmann-LaRoche & Co. Ltd., CH-4002 Basel, Switzerland **A benzo(a)quinolizine derivative with a neuroleptic-like action on cerebral monoamine turnover.** Journal of Pharmacology and Experimental Therapeutics. 203(3):556-563, 1977.

To examine the effects of a new benzo(a)quinolizine derivative, Ro 1-9564 (2-hydroxy-3-ethyl-9,10-methylenedioxy-1,2,3,4,6,7-hexahydro-11bH-benz (a)quinolizine-HCl), on cerebral monoamine turnover, a series of in vivo and in vitro animal studies were undertaken. Ro 1-9564 caused a marked increase of homovanillic acid (HVA), enhanced the elevation of 3,4-dihydroxyphenylalanine induced by 3-hydroxybenzylhydrazine as well as the alpha-methyl-p-tyrosine induced decrease of dopamine (DA). The drug did not lower the endogenous DA content to a major extent. The cerebral content of 5-hydroxyindoleacetic acid and 3-methoxy-4-hydroxyphenylethyleneglycol-SO4 was also increased by Ro 1-9564, but less markedly than that of HVA, and the endogenous brain 5-hydroxytryptamine was not diminished, whereas norepinephrine showed a moderate decline. Ro 1-9564 did not antagonize the DA depleting effect of reserpine and counteracted apomorphine in diminishing the 3-hydroxybenzylhydrazine induced 3,4-dihydroxyphenylalanine accumulation in

reserpine treated rats. It is concluded that Ro 1-9564 represents a new type of benzoquinolizine derivative which enhances striatal DA turnover by primarily interfering with presynaptic and/or postsynaptic DA receptors similarly to neuroleptic drugs such as haloperidol and chlorpromazine. Since benzoquinolizine derivatives with close chemical relationships may have a reserpine or neuroleptic like mechanism of action, a similarity between drug receptors at the granular and neuronal membrane, respectively, seems to exist. 22 references. (Author abstract modified)

001038 Soroko, F. E.; Mehta, N. B.; Maxwell, R. A.; Ferris, R. M.; Schroeder, D. H. Wellcome Research Laboratories, Department of Pharmacology, Research Triangle Park, NC 27709 **Bupropion hydrochloride ((+/-) alpha-t-butylamino-3-chloropropiophenone HCl): a novel antidepressant agent.** Journal of Pharmacy and Pharmacology (London). 29(12):767-770, 1977.

Chemical structure and pharmacokinetics of (+/-) alpha-t-butylamino-3-chloropropiophenone hydrochloride (bupropion HCl), a novel antidepressant agent, are reported together with in vivo and in vitro data on biochemical, cardiovascular, and autonomic actions and toxicity. Results indicate that bupropion HCl is active in antidepressant screening models, differs chemically and pharmacologically from the tricyclics, and is neither sympathomimetic, cholinolytic, nor an inhibitor of monoamine oxidase. 15 references.

001039 Stagg, C. J. Smith & Nephew Pharmaceuticals Ltd., Bessemer Road, Welwyn Garden City, Herts., England **Modification of the time-course of DMPEA toxicity in the mouse by centrally acting drugs.** Neuropharmacology (Oxford). 16(12):881-884, 1977.

To determine whether compounds with known antischizophrenic activities could be discriminated from other drugs by their antagonism of dimethoxyphenylethylamine (DMPEA), survival times of Porton mice without or with pretreatment with a centrally acting drug were assessed following intraperitoneal injection of a lethal dose of DMPEA. Reserpine (24 hr), haloperidol, perphenazine, and trifluperidol were found to prolong survival time; while amphetamine, phenytoin, chlorimipramine, phenelzine, pimozide, spiroperidol, and imipramine reduced survival time. Morphine, chlorpromazine, oxypertine, promethazine, and reserpine (1 hr) were inactive. A limited, but novel, classification of the tranquilizers and other psychotropic compounds may be possible according to whether they potentiate, antagonize or have no effect on the toxicity of DMPEA. 12 references. (Author abstract modified)

001040 Uyeno, Edward T.; DeGraw, Joseph I.; Johnson, Howard L.; Lawson, John A.; Loew, Gilda H. Stanford Research Institute, Menlo Park, CA 94025 **Evaluation of pure diastereomers of N-sec-alkylmorphinoids.** Pharmacologist. 19(2):157, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the agonist and antagonist properties of the isolated diastereomers of N-sec-butylnormorphine and N-alpha-methylallylnormorphine was reported. The mouse tail flick test and the phenylquinone writhing experiment revealed that each of the pure diastereomers had analgesic effects. The narcotic antagonist properties of the diastereomers were determined by the test of inhibition of Straub tail reaction. The potency ratio test indicated that the major (S) isomer of each diastereomer was significantly different in antagonistic potency from the corresponding minor (R) isomer. Opiate receptor binding data were consistent with the antagonist properties and with the isomeric antagonistic potencies. It is posited that the configuration of the diastereomer is an important variable in the structure/activity relationship of the N-sec-alkylmorphinoids. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

001041 Ackerman, Neil R. Institute of Biological Sciences, Syntex Research, Palo Alto, CA 94304 **The lack of an effect of delta9-THC on pulmonary smooth muscle function in the guinea pig.** Toxicology and Applied Pharmacology. 41(2):321-328, 1977.

The effect of delta9-tetrahydrocannabinol (THC) on bronchodilator and antiasthmatic activity was investigated in the guinea-pig to determine if it were either a bronchial smooth muscle relaxant or an antagonist of one or more of the allergic mediators. Tracheae from female Hartley strain guinea-pigs were removed, cut spirally, suspended in vitro, and isometric tension was determined with a force displacement transducer. Delta9-THC was added to the bath to determine its inherent smooth muscle relaxant activity. Cumulative log concentration response curves were obtained for histamine and acetylcholine in the absence and presence of delta9-THC. Pulmonary mechanics were determined in anesthetized spontaneously breathing and artificially respired guinea-pigs Delta9-THC was tested as an antagonist of the acetylcholine induced and histamine induced increase in airway resistance. Delta9-THC, .000001 to .01M, did not affect the tone of the tracheal strip; at .000001 to .0001M it had no significant effect on the response to acetylcholine or histamine. Intravenous administration of delta9-THC, 0.5, 1.0, and 10mg/kg did not alter the bronchoconstriction induced by histamine or acetylcholine. Results demonstrate that delta9-THC is not a pulmonary smooth muscle relaxant nor does it possess antihistaminic or anticholinergic activity. 25 references. (Journal abstract modified)

001042 Adler, Michael. State University of New York at Buffalo, Buffalo, NY **Actions of atropine and scopolamine on the endplate current of the frog sartorius muscle. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-19409 HC$15.00 MF$7.50 235 p.

To test two kinetic models of receptor/transmitter/drug molecule interactions, the effects of atropine sulphate and scopolamine hydrobromide were investigated on the endplate current (EPC) of glycerol treated frog sartorius muscle by standard voltage clamp techniques. Drug induced alterations of the EPC time course suggest these drugs act on a regulatory channel or on the channel itself to alter kinetics and voltage sensitivty of ion translocation. It was postulated that the drugs interact with receptors following their interaction with the transmitter to form a relatively stable ternary complex of transmitter/receptor/drug molecule. This ternary complex is inactive regardless of the drug used; and dissociation occurs by removal of the drug and restoration of the activated complex rather than by the unimolecular dissociation to acetylcholine, receptor, and drug molecule. Theoretical EPCs predicted by this model agree with experimental decay values. (Journal abstract modified)

001043 Airaksinen, M. M.; Huang, J-T.; Ho, B. T., Taylor, D. Department of Pharmacology, University of Kuopio, Kuopio,

Finland **Uptake of 5-methoxytryptoline (6-MeO-tetrahydro-beta-carboline) by blood platelets and its effect on 5HT uptake and release.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):39, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the uptake of 5-methoxytryptoline (6-methoxy-1,2,3,4-tetrahydro-beta-carboline) (MTC), the condensation product of 5-methoxytryptamine and formaldehyde, was studied in rabbit blood platelets in vitro to clarify its specificity to 5-HT mechanisms. MTC was rapidly and actively taken up by platelets. 5-HT and ouabain inhibited its uptake and MTC competitively inhibited the high activity uptake of 5-HT. The slow passive uptake of 5-HT was inhibited only at very high concentrations of MTC. Intracellular distribution of 14C-MTC differed from that of 14C-5-HT. High concentrations of MTC increased the spontaneous release of newly taken up 5-HT but small concentrations slightly decreased it. It was concluded that an active uptake into 5-HT neurons and the effect on 5-HT uptake may explain the specific actions of MTC.

001044 Aldridge, Andrew; Parsons, William D.; Neims, Allen H. Dept. of Pharmacology & Therapeutics, McGill University, 3655 Drummond St., Montreal, Quebec H3G 1Y6, Canada **Stimulation of caffeine metabolism in the rat by 3-methylcholanthrene.** Life Sciences (Oxford). 21(7):967-974, 1977.

The effects of phenobarbital and 3-methylcholanthrene pretreatment on the pharmacokinetic profile of caffeine in the rat was investigated. Groups of adult male rats treated with 3-methylcholanthrene, phenobarbital or vehicles alone, were administered caffeine. Serum caffeine concentrations were measured by radioimmunoassay. In vehicle and phenobarbital pretreated animals, caffeine elimination kinetics were nonlinear. Phenobarbital pretreatment did not change the apparent Km but slightly increased the apparent Vmax. 3-Methylcholanthrene pretreatment dramatically altered the elimination kinetics of caffeine. Results are consistent with the proposed involvement of the cytochromes P-450 monooxygenase system in the elimination of caffeine. In addition, results suggest that caffeine is a moderately poor substrate for the cytochrome P-450 present in control and phenobarbital pretreated rats, but a particularly good substrate for the form induced by 3-methylcholanthrene. 23 references. (Journal abstract modified)

001045 Andreoli, V.; Campedelli, A.; Maffei, F. Ospedali Neuropsichiatrici di Verona, Settore Capoluogo, Reparto Misto, Verona, Italy **/S-adenosyl-L-methionine (SAMe) treatment in gerontopsychiatry: a controlled clinical study in depressed aged patients./** La S-adenosil-L-metionina (SAMe) in geropsichiatria: uno studio clinico controllato "in aperto" nelle sindromi depressive dell'eta senile. Giornale di Gerontologia (Firenze). 25(3):172-180, 1977.

The action of S-adenosyl-L-methionine (SAMe) in a group of 17 depressed geriatric patients was investigated. Average age of the 12 males and 5 females was 66 years, and the controlled study lasted 15 days. The Brief Psychiatric Rating Scale of Overall-Gorham, the Hamilton Rating Scale, and the Geriatric Rating Scale were used to determine antidepressant effect. Results showed SAMe to be therapeutically effective as an antidepressant, that it exhibits psychostimulating and blocking action, and it is well tolerated. A decline in anxiety and somatic symptoms was also noted. 9 references.

001046 Angel, A.; Clarke, K. A.; Dewhurst, D. G. Department of Physiology, University of Sheffield, Sheffield S10 2TN, Yorkshire, England **A pharmacological study of the spontaneous convulsive activity induced by 1,2-dihyroxybenzene (catechol) in the anaesthetized mouse.** British Journal of Pharmacology (London). 61(3):433-439, 1977.

The convulsive activity induced by 1,2-dihydroxybenzene was examined in the anesthetized mouse either by determining the CD50 for the convulsions in drug treated and control animals or by studying the effects of pargyline HCl, iproniazid PO4, reserpine, L-dopa, parachlorophenylalanine (PCPA), PCPA plus 5-hydroxytryptophan, 6-hydroxydopamine, and atropine on total whole body activity. The results indicate that catecholamines play no part in the mechanism of action of catechol. Drugs which alter cerebral catecholamine levels had no effect on the convulsions, nor did the alpha and beta-adrenoceptor blocking drugs. 5-Hydroxytryptamine (5-HT) could possibly be important, though results with drugs which either change brain 5-HT levels, or block 5-HT receptors were inconsistent. Gamma-aminobutyric acid also appears not be involved in the mechanism of action of catechol. The results strongly suggest that catechol primarily activates a central cholinergic system, in that muscarinic and nicotinic receptor blocking drugs inhibit, and anticholinesterases potentiate the convulsions. 47 references. (Author abstract modified)

001047 Annunziato, L.; Gudelsky, G. A.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **The effects of hypothalamic deafferentation on the haloperidol induced activation of tuberoinfundibular dopamine neurons.** Pharmacologist. 19(2):222, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of hypothalamic deafferentation on the haloperidol induced activation of tuberoinfundibular dopamine (DA) neurons was reported. A hypothalamic island including tuberoinfundibular DA neurons was made in the rat brain. Norepinephrine concentrations were reduced 50%, but DA concentrations were unaltered, in the median eminence and hypothalamic island 15 da to 33 da after hypothalamic deafferentation. Serum prolactin concentrations in the animals were elevated 16 hr after the injection of haloperidol and 1 hr after alpha-methyltyrosine (AMT) indicating that the pituitary and hypothalamic mechanisms governing prolactin secretion were still functional. Hypothalamic deafferentation did not alter the ability of haloperidol to increase DA turnover in the median eminence, as determined from the AMT induced decline of the DA concentrations. It is suggested that the haloperidol induced, prolactin mediated increase in DA turnover in the median eminence may result from a direct action of prolactin on tuberoinfundibular DA neurons. (Author abstract modified)

001048 Atweh, Samir F.; Kuhar, Michael J. Department of Neurology, Massachusetts General Hospital, 32 Fruit Street, Boston, MA 02114 **Autoradiographic localization of opiate receptors in rat brain. III. The telencephalon.** Brain Research (Amsterdam). 134(3):393-405, 1977.

Opiate receptor distribution, determined by the autoradiographic localization of stereospecific (3H)diprenorphine bindings sites, was examined in the telencephalon of rat. Areas showing very dense or dense localization of receptors included parts of the presubiculum and amygdala, patchy areas in the caudate-putamen and accumbens, the subfornical organ, the interstriatal nucleus of the striae terminalis and the anterior olfactory nucleus, pars externa. Lower densities were found in

other parts of the hippocampal formation, the deeper part of the cerebral cortex, the entopeduncular nucleus, globus pallidus, nucleus triangularis septi and nucleus paratenialis. The significance of these finds is discussed in terms of the biochemical and physiological actions of opiates. 46 references. (Author abstract)

001049 Aubineau, Pierre; Sercombe, Richard. Laboratoire de Physiologie et de Pathologie Cerebrovasculaire, Hopital Lariboisiere, Paris, France **Evidence for a double cholinergic mechanism capable of reducing the tone of cerebral arteries.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):296-297, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, experiments designed to verify in vivo a double cholinergic mechanism capable of reducing the tone of cerebral arteries were reported. In 13 rabbits chronically implanted, cerebral blood flow (CBF) in the caudate nucleus, arterial oxygen and carbon dioxide, and blood pressure were measured. Stimulation and blocking of the superior cervical ganglion were performed, and carbachol was infused before, during, and after stimulation. The drug induced dose dependent rises in CBF in the caudate nucleus which could be inhibited with atropine, but stimulation with carbachol revealed an inhibitory effect which was reversible and not blocked by atropine. Carbachol did not inhibit reduction in CBF induced by noradrenaline. It was concluded that the cholinergic system may act in two ways to reduce the tone of cerebral arteries: by direct action on muscarinic receptors of the arterial smooth muscle and by inhibition of the sympathetic system via nonmuscarinic receptors. 4 references.

001050 Baudry, Michel; Martres, Marie-Pascale; Schwartz, Jean-Charles. Unite 109 de Neurobiologie, Centre Paul Broca de l'INSERM, 2ter, rue d'Alesia F-75014 Paris, France **In vivo binding of 3H-pimozide in mouse striatum: effects of dopamine agonists and antagonists.** Life Sciences (Oxford). 21(8):1163-1170, 1977.

The effects of dopamine agonists and antagonists on in vivo binding of (3H)pimozide in mouse striatum is studied. Evidence indicates that (3H)pimozode injection results in a specific binding of the neuroleptic to dopaminergic receptors. (3H)pimozide is preferentially accumulated in the striatum as compared to nondopaminergic structures like the cerebellum. The selective accumulation of (3H)pimozide is prevented by prior administration of various neuroleptics as well as by apomorphine. Moreover, doses of antagonist which prevent this accumulation were identical to those which lead to an increased striatal homovanillic acid level. (3H)pimozide accumulation is not modified by the administration of a variety of nondopaminergic agents. However, (3H)pimozide binding is not prevented either by indirect dopamine agonists and is even greatly increased by d-amphetamine at high doses. The possibility that direct or indirect dopamine agonists may favor the binding of the antagonist through a modification of receptor sites is discussed. 17 references. (Author abstract modified)

001051 Baweja, R.; Sokoloski, T. D.; Patil, P. N. College of Pharmacy, Ohio State University, Columbus, OH 43210 **Competitive binding between cocaine and various drugs to synthetic levodopa melanin.** Journal of Pharmaceutical Sciences. 66(11):1544-1547, 1977.

The interactions of several drugs with synthetic levodopa melanin were studied by measuring their relative tendency to compete with radiolabeled cocaine for sites on the polymer. The binding of cocaine to melanin followed a Type I Langmuir adsorption isotherm in the absence of added compounds. Cocaine, in the presence of dextronorepinephrine, levonorepinephrine, dextroamphetamine, levamfetamine, levoephedrine, dopamine, cyclopentolate, tropicamide, and possibly desipramine, conformed to a Type I adsorption relationship modified to account for competitive binding. Chlorpromazine, promazine, fluphenazine, thioridazine, imipramine, and chloroquine gave results that were not explainable by a model based on competitive inhibition of cocaine binding. However, promazine and chloroquine gave results conforming with the competitive inhibition model. The overall results indicated that some phenothiazine derivatives exhibited the greatest affinity for melanin, while the sympathomimetic amines exhibited the least affinity. 13 references. (Author abstract modified)

001052 Beaubien, A. R.; Pakuts, A. P. Drug Toxicology Division, Health Protection Branch, Health and Welfare, Ottawa, K1A 0L2, Canada **First-pass elimination of 14C-imipramine in isolated perfused rat liver.** Pharmacologist. 19(2):128, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the kinetics of radiolabeled imipramine (IP) in isolated perfused rat liver was reported. IP and desmethylimipramine (DMI) were completely absent in the hepatic vein perfusate in doses up to 1 microgram/ml. The 10 microgram/ml dose caused a marked increase in liver resistance and a decrease in biliary flow rate. As the dose increased from 0.1microgram/ml to 3.16 microgram/ml, the percentage of total administered radioactivity increased in the liver, decreased in the bile, and remained approximately constant in the hepatic vein perfusate. The major portion of liver radioactivity existed as IP and DMI at all doses. It is suggested that the results indicate that liver binding in addition to metabolism is an important mechanism for sequestering IP and DMI during first pass elimination. It is also probable that in therapeutic dose ranges, the only IP to escape the first pass effect must be that which is bound to plasma proteins and erythrocytes. (Author abstract modified)

001053 Becker, Bruce M.; Reid, Larry D. Bradley University, Peoria, IL 61606 **Daily 1-delta9-tetrahydrocannabinol and pressing for hypothalamic stimulation.** Bulletin of the Psychonomic Society. 10(4):325-327, 1977.

The effects of daily 1-delta9-tetrahydrocannabinol (THC) on pressing for intracranial stimulation (ICS) were retested in rats. Rats were fixed with chronically indwelling bipolar electrodes then trained to leverpress for ICS. They pressed twice a day for three intensities of ICS for 5 min at each intensity. On each day for 10 days prior to tests with ICS, one group of rats was given THC (10mg/kg, orally) and the other a placebo. The THC led to reduced pressing with initial doses but not with the later doses. Rats with electrode tips in the lateral hypothalamus near the entopeduncular nucleus of the internal capsule showed accelerated pressing toward the end of the 10 days of testing under THC. It is suggested that further research with THC and pressing for ICS could lead to the specification of those sites of ICS that are especially responsive to THC as reflected by acceleration of pressing for ICS. 14 references. (Author abstract modified)

001054 Beckett, A. H.; Gibson, G. G. Department of Pharmacy, Chelsea College, University of London, Mansea Road, London SW3 6LX, England **Identification of the in vitro N-oxidized metabolites of (+)- and (-)-N-benzylamphetamine.** Journal

of Pharmacy and Pharmacology (London). 29(12):756-760, 1977.

To identify the in vitro N-oxidized isomeric hydroxylamine metabolites of (+)- and (-)-N-benzylamphetamine, the techniques of gas liquid chromotography, thin layer chromatography, and combined gas liquid chromatography and mass spectrometry were used following incubation of the amphetamines with rabbit liver homogenates, and results were compared with those from reference samples. Both (+)- and (-)-N-benzyl-N-hydroxyamphetamines were identified. An additional novel metabolic product was identified after incubation of N-benzylamphetamine which had properties consistent with that of N-benzylamphetamine nitrone. 20 references. (Author abstract modified)

001055 Berndt, W. O.; Ho, I. K. Department of Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson, MS 39216 **Effects of morphine sulfate on renal transport processes.** Pharmacologist. 19(2):136, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of morphine sulfate (MS) on renal transport processes and renal cortical electrolytes in mice was reported. Twenty four hr after implantation of a pellet containing 75mg morphine alkaloid, the uptake of para-aminohippurate (PAH), tetraethylammon (TEA), and alpha-aminoisobutyrate were significantly suppressed. Tissue potassium was reduced and tissue sodium was elevated. At 72 hr, only the uptake of TEA was significantly suppressed. MS added in vitro to fresh tissue slices had no effect on organic transport or on inorganic electrolyte levels. MS administered at a dose of 40mg/kg three times at 8 hr intervals was also without effect. A single dose of 40mg/kg MS produced a significant reduction in PAH accumulation 6 hr after dosing; complete recovery occurred by 12 hr after administration. The data suggest that MS affects renal transport and that mechanisms exist for recovery from these effects even in the presence of continued administration of MS. (Author abstract modified)

001056 Beymer, Charles H.; Quock, Raymond M. Dept. of Physiology, Univ. of the Pacific School of Pharmacy, Stockton, CA 95211 **Molindone: an apomorphine antagonist in the rabbit.** Communications in Psychopharmacology. 1(4):385-392, 1977.

Studies were conducted to determine whether molindone, a dihydroindoline compound with antipsychotic properties, might antagonize compounds thought to stimulate central dopamine receptors. Pretreatment of rabbits with molindone antagonized the hyperthermic response to apomorphine but not to lysergic acid diethylamide or to fenfluramine. The temperature elevating action of amphetamine was also highly resistant to doses of molindone which abolished apomorphine hyperthermia. Higher doses of molindone only slightly reduced the magnitude of the amphetamine response. Data demonstrate that molindone can block dopamine but not serotonin receptors in the rabbit and apparently antagonizes the effects of apomorphine more effectively than the actions of amphetamine. 11 references. (Author abstract modified)

001057 Bhargava, Hemendra N.; Kasabdji, Dyabra. Department of Pharmacognosy and Pharmacology, University of Illinois at the Medical Center, Chicago, IL 60612 **Effect of mianserine on brain serotonin turnover in mice.** Research Communications in Chemical Pathology and Pharmacology. 17(4):735-738, 1977.

A study of the effects of mianserine on brain serotonin turnover in mice is described. One hr after mianserine administration brain 5-HT concentration was reduced, the greatest decrease was observed with 2.5mg/kg dose. This reduction lasted for 1 hr. Brain 5-HT turnover was increased by all doses of mianserine used. The increase in brain 5-HT turnover after a single injection lasted for 8 hr. This increase may be related to inhibition of central 5-HT receptors. 7 references. (Author abstract modified)

001058 Bielicki, L.; Krieglstein, J. Inst. fur Pharm. und Tox. im FB Pharm. und Lebensmit., Philipps-Univ., Deutschhausstrasse 17a, D-3550 Marburg/Lahn, Germany **The effect of anesthesia on brain mitochondrial hexokinase.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 298(3):229-233, 1977.

A study was undertaken to demonstrate that the distribution equilibrium between the less active soluble and the more active mitochondrial cerebral hexokinase is influenced by anesthesia. The following drugs were administered to male Sprague-Dawley rats to produce general anesthesia: phenobarbital, hexobarbital, chloral hydrate, ketamine, urethane, halothane and ether. All drugs used caused a significant increase of the less active soluble form of hexokinase in brain. Incubation of mitochondrial hexokinase with anesthetics in vitro led, except with ketamine, to an increase of the soluble enzyme form. This indicates a possible direct action of drugs on the mitochondrial membrane; however an indirect effect mediated by physiological substrates is not excluded. These findings support the hypothesis that anesthetics may inhibit glucose phosphorylation in brain by solubilizing the more active mitochondrial hexokinase. 20 references. (Author abstract modified)

001059 Blei, Ira. Division of Pure and Applied Sciences, College of Staten Island, Staten Island, NY 10301 **Effects of adenine nucleotides on oxidation of phenothiazine tranquilizers.** Journal of Pharmaceutical Sciences. 66(11):1575-1578, 1977.

The effects of adenosinediphosphate and adenosinetriphosphate on the periodic acid oxidation of the phenothiazine drugs were studied. The principal effect was a marked reduction in the rate of formation and decay of the drug free radical. The oxidation rates of the nucleotide free drugs seemed to be most strongly influenced by the inductive effects of substituents at the 2-position of the phenothiazine nucleus. However, the oxidation rates of the drugs in the presence of nucleotide were most strongly influenced by the substituents at the 10-position. Variations of the structure of substituents at the 10-position have only a modest effect on the electronic state of the phenothiazine nucleus. It is suggested that the marked effect of structural variation in the 10-position substituents in the presence of nucleotide on the periodate oxidation rate is most likely an expression of steric effects related to an interaction between drug and nucleotide. 9 references. (Author abstract modified)

001060 Boadle-Biber, M. C. Medical College of Virginia, Richmond, VA 23298 **Activation of tryptophan hydroxylase by depolarization: role of calcium.** Pharmacologist. 19(2):235, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effect of depolarization on tryptophan hydroxylase (Try-H), the rate limiting enzyme in serotonin (5-HT) synthesis, was reported. Slices of brain tissue were incubated in control or high potassium (K) medium. Depolarization with K increased Try-H activi-

ty up to 100%. No increase in activity occurred with depolarization in a solution containing the same concentration of K but no calcium (Ca). Incubation in control medium containing ouabain, or in a sodium free medium also enhanced Try H activity. It is suggested that the results: 1) show that Try-H activity increases during depolarization; 2) are consistent with the enhanced 5-HT synthesis observed in vivo during nerve stimulation; and 3) indicate that Ca may have a role in the activation process. 2 references. (Author abstract modified)

001061 Boakes, R. J.; Martin, I. L.; Mitchell, P. R. MRC Neuropharmacology Unit, The Medical School, Birmingham 15, England **Burst firing of cerebellar Purkinje neurones induced by benzodiazepines.** Neuropharmacology (Oxford). 16(10):711-713, 1977.

Burst firing of cerebellar Purkinje neurons induced by benzodiazepines was studied in urethane anesthetized rats. Iontophoretic applications of chlordiazepoxide and nitrazepam and systemic applications of flurazepam in the rats caused or increased the number of high frequency bursts of spikes and silent periods of the Purkinje neurons. These results are discussed in terms of GABA inhibitory mechanisms. 7 references. (Author abstract modified)

001062 Boggan, William O.; Meyer, Jerrold S.; Steinberg, Robert M.; Worthington, Curtis. Dept. of Psychiatry, Medical University of South Carolina, Charleston, SC 29401 **The effects of methaqualone on the seizure susceptibility of mice.** Psychopharmacology (Berlin). 54(1):45-49, 1977.

The effects of methaqualone on the seizure susceptibility of mice were studied, specifically addressing whether earlier reports of protection by methaqualone against pentylenetetrazal and electrically induced seizures could be confirmed, and whether methaqualone also antagonizes sound induced seizures. It was found that methaqualone produces dose and time dependent decreases in susceptibility to electrically, chemically, and sound induced seizures. The antagonism of methaqualone to electroconvulsive shock was dissociated from its effects on temperature regulation and plasma corticosterone. Studies with SKF525A, a drug known to block enzymes in the liver that metabolize drugs, suggest that methaqualone, rather than a metabolite produced in the liver, is responsible for its anticonvulsant effects. Tolerance to the anticonvulsant effects of methaqualone was also demonstrated. 27 references. (Author abstract modified)

001063 Borison, R.; Diamond, B.; Havdala, H.; Davis, J. M. Illinois State Psychiatric Institute, Chicago, IL 60612 **Central pharmacology of a new antidepressant.** Pharmacologist. 19(2):155, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study in which the pharmacological effects of wellbatrin (WB), an antidepressant drug which may have a rapid onset of antidepressant effects, were compared with those of dextroamphetamine and phenylethylamine (PEA), an endogenous amphetamine-like stimulant whose urinary excretion is decreased in depression, was reported. Unlike amphetamine and PEA, WB failed to produce stereotyped behavior; however, all three agents elicited stereotypy in rats made tolerant to morphine. In rats with unilateral 6-hydroxydopamine lesions of the substantia nigra, all three agents caused ipsilateral turning which was blocked by haloperidol but not by clozapine. Amphetamine and PEA, but not WB, reversed the reserpine syndrome in rats. In mice, WB produced an increase in locomotor activity which was blocked by the catecholamine depletor alpha-methyl-paratyrosine (AMT) and antagonized by the specific PEA depletor alpha-methyldopa hydrazine (MDH). The behavioral effects of WB were not potentiated or prolonged by the monoamine oxidase inhibitor pargyline. In maximal electroshock tests in mice, WB exerted clear anticonvulsant effects which were not blocked by AMT but were antagonized by MDH and reserpine. It is suggested that the central actions of WB are mediated in part by both catecholamines and by PEA. (Author abstract modified)

001064 Boulu, Roger G.; Plotkine, Michel; Gueniau, Claude. Laboratoire de Pharmacodynamie, Universite Rene-Descartes, 75006 Paris, France **Effect of dopaminergic agonists upon oxygen availability for cerebral cortex.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):352-353, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, the influence of dopamine and other dopaminergic agonists upon cortex O2 availability was studied by measurement of cortical O2 tension in unanesthetized rabbits chronically implanted with platinum electrodes in frontal cortex. L. dopa, d-amphetamine, apomorphine, and piribedil induced an increased cortical oxygen tension, and dopamine was inefficient. Apomorphine and d-amphetamine produced a concomitant increase of cerebral blood flow. These oxygen tension increases were suppressed by dopaminergic receptor blockade by haloperidol and pimozide, and could be abolished by administration of phenoxybenzamine. Findings indicated that dopaminergic cerebral mechanisms could influence O2 supply regulation. 7 references.

001065 Brookman, Sheldon; Kourounakis, Panos. Institut de Medecine et de Chirurgie Experimentales, Universite de Montreal, Montreal, Quebec H3C 3J7, Canada **Alterations induced in distribution and in vivo metabolism of imipramine by pregnenolone-16alpha-carbonitrile.** Journal of Pharmaceutical Sciences. 66(10):1492-1494, 1977.

Female rats were given pregnenolone-16alpha-carbonitrile (I) to investigate its in vivo effects on the loss of the righting reflex and the mortality rate induced by imipramine as well as the concentrations of this drug and its metabolite, desipramine, in plasma, brain, liver, lungs, and kidneys. The protective action of I was associated with diminished organ levels of imipramine (catatoxic mechanism), and the relationship between brain and plasma imipramine concentrations remained unaltered. Desipramine/imipramine molar ratios were increased, indicating an elevated rate of N-demethylation. The unbound imipramine in plasma was diminished, but the relationship between protein bound and unbound imipramine levels was not modified. 23 references. (Author abstract)

001066 Burks, Thomas F.; Grant, J. Kirkland; Rosenfeld, Gary C. Department of Pharmacology, University of Texas Medical School at Houston, Houston, TX 77030 **Cholinergic inhibition of morphine-induced hypothermia.** Pharmacologist. 19(2):170, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of cholinergic agonists on morphine induced hypothermia in the rat was reported. Injections of carbachol into a lateral cerebral ventricle (ICV) inhibited subsequent hypothermic responses to morphine and exaggerated the secondary hyperthermia which

sometimes follows the hypothermic response. The antimorphine effects of carbachol were apparent within 1.5hr and persisted up to 24 hr. Carbachol did not inhibit hypothermic responses to ICV norepinephrine, 5-hydroxytryptamine, or dopamine. The initial hypothermic response to carbachol was not blocked by naloxone, but was blocked by ICV atropine. Atropine also blocked the antimorphine effect of carbachol, but did not block the hypothermic responses to morphine. It is concluded that cholinergic substances administered ICV render the central thermoregulatory apparatus of the rat less sensitive to the hypothermic effects of morphine. (Author abstract modified)

001067 Buterbaugh, Gary G. Dept. of Pharmacology and Toxicology, School of Pharmacy, University of Maryland, Baltimore, MD 21201 **A role for central serotonergic systems in the pattern and intensity of the convulsive response of rats to electroshock.** Neuropharmacology (Oxford). 16(10):707-709, 1977.

To elucidate the role of central serotonergic systems in the patterns and intensity of the convulsive response of rats to electroshock, the effects of various drugs in nonextensor rats compared to extensor rats were studied. Rats were housed and maintained on light and dark cycles and classified with four consecutive maximal electroshock stimulation (MES) stimulii at 48 hr intervals as extensors or nonextensors. Results showed that nonextensor rats responded to MES with typical hind limb extension (HLE) after resperpine, p-chlorophenylalanine (pCPA), and digitoxigenin (DIGT) but not after alpha-methyl-p-tyrosine or pentylenetetrazol; only DIGT increased convulsive intensity. In pCPA pretreated nonextensors, DIGT increased convulsive intensity to the same degree as in untreated extensors. Since nonextensors had a significantly greater whole brain serotonin concentration than extensors, the results indicate that the atypical MES hindlimb response of nonextensors is related to quantitative and/or qualitative differences in central serotonergic systems. 10 references. (Author abstract modified)

001068 Buttar, H. S.; Frank, G. B. Food and Drug Directorate, Health and Welfare Canada, Ottawa, Ont., Canada **Effects of antipsychotic drugs on action potential production in skeletal muscle. I. Chlorpromazine and promethazine.** Canadian Journal of Physiology and Pharmacology (Ottawa). 55(3):452-461, 1977.

The effects of chlorpromazine, an antipsychotic phenothiazine, and promethazine, an antihistaminic phenothiazine, on excitability and action potential production in frog's sartorius muscle fibers were studied and compared. Both drugs produced a local anaesthetic effect which developed slowly over 3 to 5 hours with lower concentrations and was only partially reversed by exposing the muscles to a drug free solution for 3 to 4 hours. Both drugs depressed excitability and the rising phase of the action potential by inhibiting the specific increase in sodium conductance which normally follows an adequate stimulus. The qualitativity identical and the quantitatively similar effects of these two drugs would suggest that the antipsychotic effect produced by some of the phenothiazines is unrelated to their effects on action potential production. 21 references. (Author abstract modified)

001069 Candy, J. M.; Key, B. J. MRC Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **A presynaptic site of action within the mesencephalic reticular formation for (+)-amphetamine-induced electrocortical desynchronization.** British Journal of Pharmacology (London). 61(3):331-338, 1977.

To determine if (+)-amphetamine has a presynaptic action on noradrenergic nerve terminals within the mesencephalic reticular formation (MRF), changes induced in the electrocorticogram by the bilateral perfusion of (+)-amphetamine into the MRF were studied in cat encephale isole preparations. (+)-Amphetamine, applied for 5 min in the MRF, mimicked the electrocortical desynchronizaton induced by the perfusion of (-)-noradrenaline (NA) or (-)-methylnoradrenaline (AMNA) into the same sites. Perfusion of 6-hydroxydopamine (6-OHDA) also induced desynchronization but, over the 1 hr perfusion period, slow wave activity gradually returned to the electrical record. Following the application of 6-OHDA the effect of (+)-amphetamine was abolished or significantly attenuated, whereas the effect of NA or AMNA was not affected. The electrocortical desynchronization induced by (+)-amphetamine could be restored if its application was preceded by perfusion with NA or AMNA. Fluorescence studies using AMNA indicated that 6-OHDA depleted noradrenergic nerve terminals near the cannulae tips. However, the terminals were still capable of taking up exogenously applied AMNA. These results suggest that (+)-amphetamine has a presynaptic action on noradrenergic nerve terminals within the MRF. 25 references. (Author abstract modified)

001070 Carpenter, David C.; Hrdina, Pavel D.; Beaubien, Arthur R. Dept. of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa K1N 9A9, Canada **Effects of phenobarbital and diazepam on imipramine-induced changes in blood pressure, heart rate and rectal temperature of rats.** Research Communications in Chemical Pathology and Pharmacology. 18(4):613-625, 1977.

To investigate the safety of anticonvulsants in doses found equipotent in suppressing imipramine induced convulsions, the effects of diazepam (1.8mg/kg) or phenobarbital (40mg/kg)following a toxic dose of imipramine (50mg/kg) on heartrate, blood pressure and body temperature were examined in male Wistar rats. Administration of imipramine alone resulted in significant decreases in blood presure, heart rate and rectal temperature. Phenobarbital or diazepam alone failed to significantly affect any of these parameters apart from a slight reduction in rectal temperature seen with phenobarbitol. Diazepam given after imipramine antagonized the imipramine induced decrease in heartrate but increased the hypotensive and hypothermic effects. Phenobarbitol failed to significantly affect the imipramine induced changes in any of the physiological parameters studied. The present data suggests that phenobarbitol may be preferable to diazepam in treatment of imipramine induced convulsions. 30 references. (Author abstract)

001071 Carr, Laurence A.; Conway, Peter M.; Voogt, James L. Department of Pharmacology, University of Louisville Health Sciences Center, Louisville, KY 40201 **Role of norepinephrine in the release of prolactin induced by suckling and estrogen.** Brain Research (Amsterdam). 133(2):305-314, 1977.

To determine whether norepinephrine is involved in the release of prolactin induced by the neural stimulus of suckling and the hormonal stimulus of estrogen, diethyldithiocarbamate (DDC) was administered to suckled, lactating rats and ovariectomized rats. When administered to suckled, lactating rats, DDC had no effect on suckling induced increase in plasma prolactin. The drug also had no effect on prolactin levels in ovariectomized rats. However, when DDC was administered to ovariectomized rats treated with estrogen to increase plasma prolactin levels, there was a fall in plasma prolactin

levels which correlated with a decrease in hypothalamic norepinephrine synthesis. It is proposed that estrogen increases noradrenergic neuron activity which in turn increases prolactin release from the pituitary. 31 references. (Author abstract modified)

001072 Catravas, J. D.; Waters, I. W.; Davis, W. M.; Walz, M. A.; Braude, M. C. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Antagonism of 3,4-methylenedioxyamphetamine (MDA) lethality by chlorpromazine in the conscious dog.** Pharmacologist. 19(2):230, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of chlorpromazine on 3,4-methylenedioxyamphetamine (MDA) induced toxicity and lethality in dogs was reported. In conscious dogs, a lethal dose of racemic MDA produced sustained elevations in body temperature and heartrate. Mean arterial pressure, left ventricular pressure, total peripheral resistance, and cardiac output were initially increased and then profoundly depressed; death occurred shortly thereafter. Arterial p02 was significantly decreased, but arterial pH and pC02 responded in a biphasic manner. In animals receiving chlorpromazine at the termination of the MDA infusion all physiological parameters showed an early return to control levels, and all animals survived. It is suggested that chlorpromazine has a definite protective effect against MDA induced lethality in the dog. (Author abstract modified)

001073 Cavanagh, R. L.; Tilson, H. A.; Gylys, J. A. Pharmacology Department, Bristol Laboratories, Syracuse, NY 13201 **Neurochemical properties of dimoxamine (D), a new psychotherapeutic agent.** Pharmacologist. 19(2):222, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study comparing the effects of dimoxamine, a new psychotherapeutic agent, with those of d-lysergic acid diethylamide (d-LSD) and R-2,5-dimethoxy-4-methylamphetamine (R-DOM) on rat brain biogenic amines was reported. Dimoxamine and R-DOM slightly decreased the steady state levels and enhanced the turnover of norepinephrine and dopamine in discrete areas of the brain. Dimoxamine increased steady state levels of serotonin (5-hydroxytryptamine, 5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in the neocortex. In the diencephalon/limbic forebrain and hindbrain, dimoxamine decreased 5-HT and elevated 5-HIAA. In contrast, R-DOM increased both 5-HT and 5-HIAA levels, and d-LSD elevated 5-HT and lowered 5-HIAA in all three brain areas. In the 5-HT sensitive isolated rat fundus strip, R-DOM had potent 5-HT-like agonist activity, while d-LSD acted as a 5-HT antagonist. Dimoxamine had a weak agonist effect, but also antagonized 5-HT and R-DOM induced spasms. It is posited that the effects of dimoxamine on the serotonergic system of the rat can be differentiated from those of d-LSD and R-DOM. 1 reference. (Author abstract modified)

001074 Ceder, G.; Schuberth, J. Psychiatric Research Center, University of Uppsala, Uppsala, Sweden **Formation of brain acetylcholine from dietary choline and the effect of barbiturate anaesthesia on this process.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):44, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the effects of pentobarbital anesthesia (PA) on the turnover of choline (Ch) in plasma and on the in vivo levels and postmortem changes of Ch and acetylcholine (ACh) were studied in mice fed a 2H-Ch diet. Plasma Ch and brain Ch and ACh was increased by PA. The dilution of 2H-Ch in the plasma Ch pool decreased and that in brain was unaffected. When the mice were compensated for the hypothermia induced by PA only an increase in brain ACh appeared. The rate of postmortem increase in brain ACh was in the PA mice one seventh and in the PA mice kept at normal body temperature one half that of controls. The postmortem decrease in brain ACh was unaffected by PA. It was concluded that the decrease in Ch turnover in plasma was due to hypothermia. Also the data indicate that the precursor of brain Ch formed in vivo is different from that formed after death. The data also suggest that excess ACh formed during PA is localized in a stable pool, perhaps in the vesicles.

001075 Cerreta, K. V.; Guerrero-Munoz, F.; Way, E. Leong. Department of Pharmacology, University of California, San Francisco, CA 94143 **Blockade of synaptosomal Ca++ uptake by opiates in vitro.** Pharmacologist. 19(2):143, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of various opiates on the calcium ion (Ca) uptake process in vitro was reported. Nerve ending fractions of mouse brain homogenates were prepared and Ca uptake was determined in untreated synaptosomes and in the presence of morphine, dextrorphan, levorphanol, or naloxone. Compared to control values, morphine decreased both the rate of Ca uptake and the maximal uptake level. Levorphanol was more effective than morphine, while dextrorphan was without effect. Naloxone did not alter the rate of Ca uptake, but slightly decreased the maximal uptake level. Naloxone also partially reversed the decrease in Ca uptake caused by morphine. It is suggested that in vivo, the effects of morphine and levorphanol on Ca uptake into the nerve ending could result in decreased neurotransmitter release. (Author abstract modified)

001076 Chau-Pham, Thuy T.; Dewey, William L. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Comparative inhibitory effects of synthetic enkephalins on the stereospecific binding of 3H-dihydromorphine and 3H-naloxone.** Pharmacologist. 19(2):189, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of methionine-enkephalin (Met) and other synthetic enkephalins on the stereospecific binding of radiolabeled dihydromorphine (DHM) and radiolabeled naloxone (NLX) in mouse brain tissue and rat brain tissue was reported. Met was more potent in inhibiting the stereospecific binding of DHM than that of NLX in mouse brain homogenates. Other synthetic peptides were also more active in inhibiting DHM binding than NLX binding in mouse brain homogenates. Met was a less potent inhibitor of DHM in washed mouse brain membranes; however, an increase in the inhibitory effects of Met on DHM binding was observed following the readdition of the supernatant to washed mouse brain membranes. This supports the hypothesis that Met may be part of a larger endogenous ligand. Met was also more potent in inhibiting DHM binding than NLX binding in rat brain homogenates. However, no difference was observed in the inhibitory effect of Met on the binding of DHM in whole rat brain homogenates or washed rat brain membranes. The use of different radiolabeled drugs (agonist vs antagonist), different species (mouse vs rat), and/or the variation in the preparation (brain homogenates vs washed membranes) are suggested as possible causes of these differences. (Author abstract modified)

001077 Cheney, D. L.; Costa, E. Lab. of Preclinical Pharmacology, National Institute of Mental Health, St. Elizabeths Hospital, Washington, DC 20032 **Pharmacological implications of brain acetylcholine turnover measurements in rat brain nuclei.** Annual Review of Pharmacology and Toxicology. 17:369-386, 1977.

New concepts in the study of the molecular dynamics of cholinergic transmission are reviewed as they developed in experiments on brain aceylcholine (ACh) turnover measurement in the rat brain nuclei. Both nonisotopic methods and isotopic methods are explained. Studies on the effects of drugs (parasympathomimetics, parasympatholytics, barbiturates, anesthetics, inhibitors of ACh synthesis, narcotic analgesics, psychotomimetics, dopamine receptor agonists, dopamine receptor blockers, GABA receptor stimulants, and central nervous system stimulants) on ACh turnover are summarized. It is concluded that the measurement of the Vmax of the low Km uptake of choline and the measurement of deuterium incorporation into cholinergic and ACh of various nuclei of rat brain, following the infusion at constant rate with deuterated phosphorylcholine, is the most successful method of measurement used in these studies. 128 references.

001078 Chesher, G. B.; Chan, B. Dept. of Pharmacology, University of Sydney, N.S.W. 2006, Australia **Footshock induced analgesia in mice: its reversal by naloxone and cross tolerance with morphine.** Life Sciences (Oxford). 21(11):1569-1574, 1977.

The action of naloxone and morphine on analgesic responses to shock in mice was investigated. Using the abdominal constriction response as the criterion for analgesia, mice tested immediately after a period of footshock showed a significant analgesic response compared with nonfootshocked controls. Footshock induced analgesia could not be elicited in mice that had been made tolerant to morphine or in mice that had been pretreated with the narcotic antagonist naloxone. It is concluded that footshock induced analgesia in the mouse is due to the release of endogenous opioid peptides. 13 references. (Author abstract)

001079 Chiueh, C. C.; Kopin, I. J. Laboratory of Clinical Science, NIMH, Bldg. 10, Room 2D-46, 9000 Rockville Pike, Bethesda, MD 20014 **Cocaine-induced centrally-mediated release of catecholamines into blood of undisturbed rats. (Unpublished paper).** Bethesda, MD, NIMH, 1977. 1 p.

The mechanism for cocaine induced centrally mediated release of catecholamines into blood of undisturbed rats was examined. Blood obtained from rats via an indwelling arterial catheter was assayed for plasma levels of norepinephrine and epinephrine using a radioenzymatic assay. After cannulation, basal levels of the catecholamines were measured. Administration of cocaine via the arterial catheter produced a dose related increase in both catecholamines. Inhibition of catechol-O-methyltransferase by tropolone increased the maximal response to cocaine 5 to 10 fold without altering significantly the basal plasma levels of norepinephrine (NE) or epinephrine. Bilateral splanchnic denervation reduced the cocaine and tropolone induced release of epinephrine and NE, but desmethylimipramine failed to alter significant plasma levels of the catecholamines. It was concluded that the increment in plasma levels of NE and epinephrine in rats given cocaine is mainly the result of a centrally mediated adrenal medullary discharge of catecholamines, rather than inhibition of uptake. (Author abstract modified)

001080 Choi, D. W.; Farb, D. H.; Fischbach, G. D. Harvard Medical School, Dept. of Pharmacology, 25 Shattuck St., Boston, MA 02115 **Chlordiazepoxide selectively augments GABA action in spinal cord cell cultures.** Nature (London). 269(5626):342-344, 1977.

The effect of chlordiazepoxide on GABA and glycine responses in spinal cord cell cultures, where individual neurons can be visualized and tested directly is analyzed. Results suggest that chlordiazepoxide selectively facilitates the action of GABA, whether exogenously applied or synaptically released, by direct action on the postsynaptic membrane. The selectivity of chlordiazepoxide as a complement to the GABA antagonists, should prove useful in identifying and characterizing GABAergic pathways in the central nervous system. 12 references.

001081 Christensson, E. G. AB Ferrosan, Malmo, Sweden **The effect of melperone (Buronil(R)) and its metabolite FG 5155 on the cyclic GMP level in rat cerebellum compared to some other neuroleptics.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):45, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the influence of melperone and its metabolite FG 5155 on the cyclic GMP (cGMP) level in rat cerebellum was compared to other neuroleptics. Drugs which increased cGMP were harmaline, apomorphine, amphetamine, picrotoxin, and oxotremorin. Drugs which decreased cGMP were diazepam, baclofen, phenoxybenzamine, almost all neuroleptics except sulpiride, which was outstanding in increasing cGMP. Propanolol and clonidine had only a very weak effect on the cGMP level. Within the tested neuroleptics chlorpromazine, thioridazine, and droperidol decreased the cGMP level most. Clozapine, melperone, and haloperidol were also potent neuroleptics in this respect, while thiothixene did not significantly change the cGMP level. FG 5155 had a tendency to increase cGMP in low doses. The deviating effect of the metabolite from melperone might be explained by the absence of a central alpha receptor blocking effect.

001082 Christoph, Greg R.; Kuhn, Donald M.; Jacobs, Barry L. Dept. of Psychology, Princeton University, Princeton, NJ 08540 **Electrophysiological evidence for a dopaminergic action of LSD: depression of unit activity in the substantia nigra of the rat.** Life Sciences (Oxford). 21(11):1585-1596, 1977.

The electrophysiological effects of LSD on the substantia nigra of the rat were investigated. The data indicated that LSD (25 to 50micrograms/kg) significantly decreased the firing rate of 78% of the dopamine containing neurons in the substantia nigra of chloral hydrate anesthetized rats. In a subgroup of neurons (22%), LSD either had no clear effect or caused a slight excitation. On the other hand, brom-LSD (100micrograms/kg), a nonhallucinogenic congener of LSD, had no effect on 71% of dopaminergic cells and slightly reduced the firing rate with 29% of the units. Pretreatment with haloperidol (0.1mg/kg) blocked the inhibitory effects of LSD, and haloperidol injected following LSD reversed its depressive effects. Nondopaminergic neurons in the region of the substantia nigra typically showed large increases in firing rate in response to LSD administration. It is asserted that the inhibitory effects of LSD on dopamine containing neurons are probably not attributable to the serotonergic properties of LSD, since 5-methoxy-N,N-dimethyltryptamine, which has central serotonergic properties similar to those of LSD, produced exclusively excitatory effects on the firing rate of dopaminergic cells. These electrophysiological results are seen

as consistent with recent behavioral and neurochemical data which suggest that LSD can act as a dopamine agonist in the CNS. 28 references. (Author abstract)

001083 Churyukanov, V. V.; Sinitsyn, L. N. Kafedra farmakologii, I Moskovskogo meditsinskogo instituta im. I. M. Sechenova, Moscow, USSR /**Effect of narcotics on conduction of afferent visceral impulses.**/ Vliyanie narkoticheskikh veshchestv na provedenie impul'sov v afferentnykh putyakh vistseral'nykh nervov. Farmakologiya i Toksikologiya (Moskva). 40(1):22-28, 1977.

Effects of noninhalation narcotics on cortical and subcortical evoked potentials with visceral, somatic, acoustic, and photostimulation were investigated in cats. With different modes of stimulation Na ethaminal was found to inhibit evoked potentials of the cerebral hemispheres, diencephalon, and midbrain cortex. Hexabarbital sodium suppressed biopotentials in specific, associative, and nonspecific brain structures with visceral and somatic stimulation. Viadril inhibited potentials in all types of stimulation. 7 references. (Journal abstract modified)

001084 Cicero, Theodore J.; Badger, Thomas M.; Wilcox, Carol E.; Bell, Roy D.; Meyer, Edward R. Department of Psychiatry, Washington University School of Medicine, 4940 Audubon Avenue, St. Louis, MO 63132 **Morphine decreases luteinizing hormone by an action on the hypothalamic-pituitary axis.** Journal of Pharmacology and Experimental Therapeutics. 203(3):548-555, 1977.

To examine the effects of morphine on the hypothalamic/pituitary axis, particularly on the secretion or synthesis of luteinizing hormone (LH), a series of studies were undertaken in normal and castrated male rats. Both acute and chronic morphine administration significantly lowered LH levels and, subsequently, testosterone. The locus of action of morphine seems to be at the level of the hypothalamus since it was found that: 1) acute morphine treatment does not alter the content of LH in the pituitary, whereas chronic administration increased the levels slightly (these data suggest that the synthesis of LH is probably not blocked by the narcotic); 2) morphine alone has no direct effect on baseline (nonstimulated) release rates of LH from the pituitary; 3) morphine does not block the effects of LH releasing factor on the secretion of LH by the pituitary, in vivo or in vitro; and 4) morphine markedly reduced the increase in serum LH levels produced by castration in the male rat. The present results suggest that morphine blocks the increase in the activity induced by castration in hypothalamic pathways. The foregoing observations, therefore, implicate the hypothalamus as the site of the disruptive action of the narcotic on reproductive endocrinology. Moreover, the observations additionally suggest that the secretion and/or synthesis of luteinizing hormone releasing factor is impaired in morphine treated animals. 25 references. (Author abstract modified)

001085 Clement-Cormier, Yvonne C. Department of Pharmacology, Neurobiology, and Anatomy, University of Texas Medical School at Houston, Houston, TX 77025 **The chemistry of dopamine receptors in the median eminence.** Pharmacologist. 19(2):202, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of various drugs on the activity of dopamine (DA) sensitive adenylate cyclase in the median eminence of mammalian brain was reported. Low levels of DA stimulated acenylate cyclase from the median eminence. The beta-adrenergic agonist l-isoproterenol had no significant effect on adenylate cyclase activity. Apomorphine, which is known to mimic the pharmacological and physiological effects of DA, stimulated adenylate cyclase from the median eminence. Representatives of several different classes of drugs effective in the treatment of schizophrenia, including the phenothiazine, butyrophenone, dibenzodiazepine, and dibenzoxazepine classes, were potent competitive inhibitors of the stimulation of the enzyme by DA. It is posited that these results, considered together with previously published data, support the hypothesis that the therapeutic effects, as well as the extrapyramidal and endocrinological side effects of these drugs, may be attributable to their ability to block the activation of adenylate cyclase in various select areas of the brain. (Author abstract modified)

001086 Collard, K. J.; Roberts, M. H. T. Dept. of Physiology, University College, P.O. Box 78, Cardiff CF1 1XL, Wales **Effects of lithium on the elevation of forebrain 5-hydroxyindoles by tryptophan.** Neuropharmacology (Oxford). 16(10):671-673, 1977.

Effects of lithium on the elevation of forebrain 5-hydroxyindoles by tryptophan was investigated on rats (n=220). Treatment with lithium for 10 days reduced the increase in forebrain 5-hydroxytryptamine concentration produced by a high dose of L-tryptophan and correspondingly increased the 5-hydroxyindole acetic acid concentration. This suggests that lithium increases the deamination of 5-hydroxytryptamine, possibly by inhibiting the storage of 5-hydroxytryptamine within neurons. Treatment with lithium for 5 days similarly reduced the increase in forebrain 5-hydroxytryptamine concentration following tryptophan, but in this case production of 5-hydroxyindole acetic acid was unaffected. These findings indicate that the apparent increase in 5-hydroxytryptamine deamination is more evident following long-term than short-term lithium treatment. 15 references. (Author abstract)

001087 Craig, J. R.; Munsat, T. L.; Chuang, M. Department of Neurology, University of Southern California School of Medicine, Los Angeles, CA **Programmed feeding as a model of chronic alcoholism in the rat.** Annals of Neurology. 2(4):311-314, 1977.

To further evaluate programmed feeding polydipsia as a model of chronic alcoholism in the rat, 18 male Charles River rats were assessed for the major behavioral and physiological criteria of an experimental model of human chronic alcoholism during a 4 week trial of programmed feeding. Programmed feeding polydipsia results in a high oral ethanol consumption and a predictable withdrawal reaction associated with audiogenic seizures. The maintenance of high blood ethanol levels for three weeks was associated with audiogenic seizures after 6 to 8 hours of withdrawal. These chronic alcoholic rats had enhanced blood clearance of ethanol. The cerebral cortical crude mitochondrial fraction showed a decrease in total and magnesium dependent adenosine triphosphatase activity in alcoholic and control (water fed) rats compared with normal rats. 15 references. (Author abstract modified)

001088 Crain, Stanley M.; Peterson, Edith R.; Crain, Bea; Simon, Eric J. Department of Neuroscience, Albert Einstein College of Medicine, Yeshiva University, Bronx, NY 10461 **Selective opiate depression of sensory-evoked synaptic networks in dorsal horn regions of spinal cord cultures.** Brain Research (Amsterdam). 133(1):162-166, 1977.

An initial demonstration that sensory evoked synaptic networks in the dorsal horn regions of spinal cord tissue cultures

can be selectively depressed by exposure to opiates, is reported. Results indicate that these sensory CNS networks may develop localized opiate inhibitory systems in vitro, consonant with increasing evidence that endorphins (i.e. endogenous opioid peptides) play a significant role in the regulation of synaptic networks in the dorsal spinal cord and a number of other specific regions of the CNS. The presence of endorphin mediated networks in isolated cord/dorsal root ganglia explants may provide clues to the biological source of these endogenous opiates, especially in view of their close relationship to pituitary hormones. 16 references.

001089 Criswell, H. E.; Dahlberg, S. T.; Cwiertniewicz, J. S. Dept. of Psychology, Williams College, Amherst, MA **Delayed onset of single dose tolerance to morphine analgesia.** Life Sciences (Oxford). 21(12):1735-1739, 1977.

To study delayed onset of single dose tolerance to morphine analgesia, rats received either 20mg/kg morphine sulfate i.p. or 5 micrograms morphine sulfate microinjected into the periaqueductal gray area of the brain. The analgesic effect of the morphine was determined by comparing preinjection and postinjection tailflick latencies. To test for tolerance following a single injection, the procedure was repeated 6, 12 or 24 hours after the first injection and tests. Tolerance was not observed 6 hours after the original injection, tolerance was observed at 12 hours and increased tolerance was present at 24 hours. Single dose tolerance to morphine appears to develop slowly over a period of several hours and during much of this time, the amount of opiate present in the brain was insufficient to produce analgesia. Similarity between central and peripheral administration suggests a central mechanism of single dose tolerance. 8 references. (Author abstract modified)

001090 Crowley, William R.; Rodriguez-Sierra, Jorge F.; Komisaruk, Barry R. Laboratory of Clinical Science, NIMH, Bldg. 10, Room 2D/46, Bethesda, MD 20014 **Analgesia induced by vaginal stimulation in rats is apparently independent of a morphine-sensitive process.** Psychopharmacology (Berlin). 54(3):223-225, 1977.

A study of vaginal stimulation induced analgesia in rats is reported, in which rats were pretreated with naloxone HCl, a potent narcotic antagonist, in order to clarify the mechanism underlying the analgesia. Pretreatment with naloxone HCl did not antagonize this vaginal stimulation induced analgesia. Furthermore, vaginal stimulation was found to exert its analgesic effect even in rats made tolerant to, and dependent upon, morphine sulfate. These results suggest that the analgesic effect of vaginal stimulation is not necessarily mediated by an opiate sensitive neural system. However, even though vaginal stimulation and other analgesic manipulations may act via different neural substrates, they may nevertheless converge onto a final common mechanism for pain suppression. 8 references. (Author abstract modified)

001091 Danielson, Terry J.; Davis, Bruce A.; Boulton, Alan A. Psychiatric Research Unit, University Hospital, Saskatoon, Sask. S7N 0W8, Canada **Species variation with respect to the metabolism and excretion of d-amphetamine and d,l-N-hydroxyamphetamine succinate.** Canadian Journal of Physiology and Pharmacology (Ottawa). 55(3):439-443, 1977.

The metabolism of amphetamine and N-hydroxyamphetamine was studied in the rat and mouse. Extensive reduction of N-hydroxyamphetamine to amphetamine occurred in both species. In addition, para-hydroxylation of amphetamine was a common metabolic route, although it was more predominant in the rat. No appreciable difference in the 24 hour excretion of amphetamine and para-hydroxyamphetamine in either species was seen after substitution of N-hydroxyamphetamine for amphetamine. 17 references. (Author abstract)

001092 David, J.; Grewal, R. S. CIBA-GEIGY Research Centre, Bombay 400063, India **Time course and development of electro-clinical features in relation to pentylenetetrazol thresholds in monkeys with focal seizures.** Life Sciences (Oxford). 21(8):1109-1116, 1977.

The differential development of focal electroencephalograph (EEG) abnormalities and pentylenetetrazol thresholds in monkeys with induced focal seizures is studied. Seizure manifestations occurred concurrently with significantly increased focal EEG abnormalities and significantly lowered pentylenetetrazol thresholds in monkeys, 69 days following standardized aluminium hydroxide injections into motor cortical sites in both hemispheres. Seizure occurrence, chemical threshold and EEG changes tended to stabilize after 145 days. Onset of epileptic changes occurred significantly faster in monkeys with motor cortical foci in both hemispheres rather than in those with unilateral foci. Focal EEG changes, viz. spike density, was inversely correlated with pentylenetetrazol thresholds to a highly significant extent. 13 references. (Author abstract modified)

001093 Davis, W. M.; Waters, I. W.; Hatoum, H. T.; Buelke, J. L.; Braude, M. C. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Triphasic dose-lethality relationships for amphetamine and certain ring-substituted amphetamines in isolated or aggregated mice.** Research Communications in Chemical Pathology and Pharmacology. 17(4):575-582, 1977.

Dose mortality curves were traced in Swiss-Webster albino mice under both isolated and aggregated (N = 5/group) conditions after intraperitoneal injections of: d-amphetamine (AMP), dl-4-methoxyamphetamine (PMA), dl-2,5-dimethoxyamphetamine, dl-2,5-dimethoxy-4-bromoamphetamine (DOB), dl-2,5-dimethoxy-4-methylamphetamine (DOM), dl-3,4-methylenedioxyamphetamine (MDA), dl-2-methoxy-4,5-methylenedioxyamphetamine (MMDA-2), and dl-2,4,5-trimethoxyamphetamine (TMA-2). Only PMA, DOM and TMA-2 did not show a triphasic dose lethality relationship under either aggregated or isolated condition. Only for AMP, MDA and TMA-2 did responses of isolated and aggregated mice differ. Thus, either of the two unusual properties of AMP regarding lethality in mice, enhancement by aggregation and the triphasic pattern, was found for certain methoxyamphetamines without the other. These two properties evidently are not derived from a common mechanism. 14 references. (Author abstract)

001094 De Giacomo, M.; Flamini, G.; Camaioni, D.; De Francisci, G.; Magalini, S. I. Istituto di Anestesiologia e Rianimazione, Universita Cattolica del Sacro Cuore, Rome, Italy **Changes in liver function in acute poisoning by barbiturate, reserpine and amphetamine.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):316-320, 1977.

In a paper presented at the 7th International Congress of the European Association of Poison Control Centres, held at Oslo, Norway during June 1976, changes in liver function in acute poisoning by barbiturates, reserpine, and amphetamine are described. Groups of 10 guinea-pigs were injected with one of the three drugs, and the following analyses were made: 1) cellular capacity to conjugate and secrete the biliary pigment through bilirubin and alkaline phosphatase analysis, 2) synthesis of some coagulation factors through the normotest, and 3)

ultrastructural morphology. Phenobarbital treatment produced the highest increase of normotest values, while increasing alkaline phosphatase serum rate only moderately. Amphetamine, phenobarbital, and reserpine cause large increases in the bilirubinemia values. 9 references.

001095 de Montigny, C.; Aghajanian, G. K. Yale University School of Medicine, Connecticut Mental Health Center, PO Box 1842, New Haven, CT 06508 **Preferential action of 5-methoxytryptamine and 5-methoxydimethyltryptamine on presynaptic serotonin receptors: a comparative iontophoretic study with LSD and serotonin.** Neuropharmacology (Oxford). 16(12):811-818, 1977.

The effects of iontophoretic application of 5-methoxytryptamine (5-MeOT) and 5-methoxydimethyltryptamine (5-MeODMT) were studied on serotonin (5-HT) containing neurones of the midbrain raphe nuclei (presynaptic area) and on neurones of two representative postsynaptic areas, the lateral geniculate body (ventral nucleus) and the amygdala (median, cortical and basolateral nuclei) of the rat which both receive a dense 5-HT input from the midbrain raphe, and the effects of 5-MeOT and 5-MeODMT were compared to that of lysergic acid diethylamide (LSD) and 5-HT applied to the same neurones. All four substances depressed neuronal firing in the three areas. Lysergic acid diethylamide, 5-MeODMT and 5-MeOT were found to exert a much more powerful effect on presynaptic (5-HT) neurones whereas 5-HT was slightly more active in depressing postsynaptic (amygdala and geniculate) neurones. The ratios of the presynaptic and postsynaptic efficacies were calculated to be 5.6, 4.3, 1.8and 0.7for LSD, 5-MeODMT, 5-MeOT and 5-HT respectively. Since a correlation between the hallucinogenic efficacy of indoleamines and their preferential presynaptic effect has been described, these results are in agreement with the reported hallucinogenic potency of 5-MeODMT and suggest that 5-MeOT could also have psychotomimetic properties. 51 references. (Author abstract)

001096 Desaiah, D.; Ho, I. K. University of Mississippi Medical Center, Jackson, MS 39216 **Catecholamine-sensitive ATPase activities in brain synaptosomes of morphinized mice.** Pharmacologist. 19(2):144, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the interaction of morphine with dopamine (DA) and norepinephrine (NE) stimulated adenosine triphosphatese (ATPase) activities in mouse brain was reported. Morphine or naloxone did not affect sodium/potassium ATPase or magnesium ATPase activities in vitro. However, morphine reduced catecholamine stimulated ATPase activities by more than 50%; this effect was blocked by naloxone. In mice rendered tolerant to morphine by pellet implantation, the synaptosomal ATPases became less sensitive to DA or NE stimulation. DA and NE stimulation of ATPase activity partially recovered upon precipitated withdrawal by naloxone and abrupt withdrawal. It is suggested that morphine may have a direct effect on catecholamine sensitive ATPase activity in mouse brain synaptosomes, and that further studies are required to determine the mechanism of enzyme stimulation by catecholamines and its interaction with morphine. (Author abstract modified)

001097 DeVore, G. R.; Woodbury, D. M. Dept. of Pharmacology, Univ. of Utah College of Medicine, Salt Lake City, UT 84132 **Phenytoin: an evaluation of several potential teratogenic mechanisms.** Epilepsia. 18(3):387-396, 1977.

The effect of pharmacological doses of phenytoin administered for a maximum of 28 days was studied in pregnant and nonpregnant rats as well as in 14 and 21 day fetuses. Pregnant animals demonstrated an increase in anticonvulsant activity as well as increased serum concentrations of phenytoin throughout pregnancy and on the 7th postpartum day. Brain concentrations of phenytoin increased during pregnancy but had returned to the values in the nonpregnant group at the 7th post partum day. Teratogenic effects of phenytoin could be related to the increased serum and tissue concentrations of the drug observed during pregnancy as well as its effect on serum folate at day 14 of gestation. 34 references.

001098 DiRaddo, Jean Strand. University of Rochester **Age-related effects of reserpine on behavior and on regional catecholamine uptake and release in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. Microfilms, No. 77-25443 HC$15.00 MF$8.50 165 p.

Age related effects of reserpine on behavior and regional catecholamine (CA) uptake and release were studied in rats 7, 10, 14, 21, 28, and 70 days old. Ss were studied after reserpine injection for locomotor activity, temperature, normal posture and eye opening, and endogenous noradrenaline levels in cortex, and recovery times were noted. In vitro uptake and release studies focused on 5 min and 20 min uptake and evoked release in cortical, hypothalamic, and striatal tissue in control and reserpine treated Ss, and age related effects were again reported. Since it has been previously shown that endogenous CA levels and terminal density increase with age, the lack of significant age related variation in control 5 and 20 min uptake found in cortical and hypothalamic samples may suggest that the endogenous CA content is less than the vesicular capacity for CA in younger animals, whereas content is closer to capacity in adults. The general lack of age related variation in evoked release suggests that the proportion of exogenous, newly taken up transmitter that is releasable generally does not change with age. For variables measured, 10 and 28 day animals generally recovered earlier from reserpine effects than 70 day animals, contradicting previous suggestions that young rats are hypersensitive to reserpine. (Journal abstract modified)

001099 Dolphin, Annette; Sawaya, M. Christina B.; Jenner, Peter, Marsden, C. David. Groupe NB, Inserum U114, College de France, F-75000 Paris, France **Behavioural and biochemical effects of chronic reduction of cerebral noradrenaline receptor stimulation.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 299(2):167-173, 1977.

The behavioral and biochemical consequences of chronic reduction of cerebral noradrenergic receptor stimulation were investigated in mice. Following chronic administration of various treatments to reduce cerebral noradrenergic function, alterations in the sensitivity of limbic forebrain adenylate cyclase to noradrenaline (NA) and in the locomotor response of the mice to dopaminergic and noradrenergic agonists were studied. An enhanced response of the NA sensitive adenylate cyclase to NA occurred after treatments producing a chronic reduction in stimulation of alpha-adrenergic receptors (phenoxybenzamine), beta-adrenergic receptors (propranolol), all noradrenergic receptors (reserpine plus the dopamine-beta-hydroxylase inhibitor FLA-63), and dopaminergic as well as noradrenergic receptors (chlorpromazine). NA stimulated adenylate cyclase sensitivity was not altered by chronic treatment with FLA-63 alone. None of the treatments except chlorpromazine increased the locomotor activity induced by

clonidine or apomorphine plus clonidine. The results support the hypothesis that noradrenergic stimulation plays a role secondary to that of dopamine in the production of locomotor activity. 43 references. (Author abstract modified)

001100 Domelsmith, L. N.; Munchausen, Linda L.; Houk, K. N. Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803 **Lysergic acid diethylamide. Photoelectron ionization potentials as indices of behavioral activity.** Journal of Medicinal Chemistry. 20(10):1346-1348, 1977.

A series of animal studies indicating that photoelectron ionization potentials of lysergic acid diethylamide (LSD) may serves as indices of behavioral activity are briefly reported. The photoelectron spectrum of LSD reveals five ionization potentials (IP's) between 7.25 and 9.75 eV arising from the aromatic portion of the molecule and IP's of 8.4eV arising from the tertiary amine and 8.5to 9.0and 9.1eV arising from the amide group. Comparisons of the IP's of LSD, and of phenethylamines and tryptamines reported elsewhere, with activities of these compounds in rat and human behavioral tests show that increasing activity is paralleled by decreasing IP. 15 references. (Author abstract modified)

001101 Dubuisson, David; Melzack, Ronald. Dept. of Psychology, McGill University, Montreal, Quebec, Canada **Analgesic brain stimulation in the cat: effect of intraventricular serotonin, norepinephrine, and dopamine.** Experimental Neurology. 57(3):1059-1066, 1977.

To further elucidate neurotransmitter influences in stimulation produced analgesia, behavioral observations and polygraph recordings were made in female cats following intraventricular injection of serotonin, dopamine, or norepinephrine. Results indicate that intraventricular dopamine and norepinephrine reduce the effectiveness of analgesic brain stimulation. The combination of serotonin plus brain stimulation produces unusual disturbances of motor tone which interfere with the pain rating system. Thus norepinephrine and dopamine are antagonistic to analgesic brain stimulation in the cat, while the findings with serotonin suggest a combination of analgesia and motor tone disruption. It is concluded that no single aminergic neurotransmitter can be equated with the neural mechanism underlying stimulation induced analgesia; rather, there appears to be a balance of serotonergic and catecholaminergic influences. 40 references.

001102 Duggan, A. W.; Hall, J. G.; Headley, P. M.; Griersmith, B. T. Dept. of Pharmacology, Australian National University, Canberra, ACT 2601, Australia **The effect of naloxone on the excitation of dorsal horn neurones of the cat by noxious and non-noxious cutaneous stimuli.** Brain Research. 138(1):185-189, 1977.

The effect of doses of naloxone previously used to reverse the effects of morphine and methionine enkephalin amide (M-ENKA) administered into the substantia gelatinosa of cats were investigated for the effect on the responses of neurons in laminae IV and V. In addition the descending inhibition of dorsal horn neurons were examined to investigate possible release of endorphins. In cats intravenous naloxone increased the nociceptive responses of 2 of 13 neurons. Observed differences after morphine and M-ENKA were the result of antagonism of exogenous substances and were not complicated by concomitant antagonism of tonically released endorphins. It is suggested that endorphins do not play a role in the tonic inhibition of dorsal horn neurons revealed by spinal cold block. 19 references.

001103 Durham, H. D.; Frank, G. B.; Marwaha, J. Dept. of Pharmacology, University of Alberta, Edmonton, Alta. T6G 2H7, Canada **Effects of antipsychotic drugs on action potential production in skeletal muscle. II. Haloperidol: nonspecific and opiate drug receptor mediated effects.** Canadian Journal of Physiology and Pharmacology (Ottawa). 55(3):462-470, 1977.

The effects of haloperidol, an antipsychotic butyrophenone, on excitability and action potential production in frog's sartorius muscle fibers were studied. The drug produced a local anaesthetic like effect which developed slowly over 1 to 5 hours with lower concentrations but was completely reversed by exposing the muscles to a drug free solution. It is suggested that haloperidol, like meperidine, suppresses action potential production by two mechanisms of action: one, a nonspecific local anaesthetic like effect; and the other a specific inhibition of sodium conductance mediated by means of an opiate drug receptor associated with the muscle fiber membrane. It is suggested that haloperidol or a related drug may be found to be more effective than methadone in treatment programs for human opiate addicts. 15 references. (Author abstract modified)

001104 Dvorchik, Barry H.; Driver, Albert G.; Jacobs, Robert A. M.S. Hershey Medical Center, Pennsylvania State University, Hershey, PA 17033 **Pharmacokinetics of hexobarbital in the pregnant and nonpregnant stumptailed monkey.** Pharmacologist. 19(2):127, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the pharmacokinetics of hexobarbital in pregnant stumptailed monkeys (Macaca arctoides) at midterm, at three quarter term, and in the same animals 8 weeks after delivery via Caesarian section was reported. At all times the pharmacokinetics of hexobarbital could be described by a two compartment open model with elimination occurring from the central compartment. Changes in the volumes of distribution, half-life, elimination rate constant, and total body clearance of the drug were observed during pregnancy. Hexobarbital half-life and sleeping time were greatest at midterm and least 8 weeks after delivery. The total body clearance of the drug was lower, and plasma protein binding was greater, during pregnancy than at 8 weeks after delivery. (Author abstract modified)

001105 Ebadi, M.; Bifano, J.; Klangkalya, B.; Govitrapong, P.; Durham, P. Department of Pharmacology, University of Nebraska College of Medicine, Omaha, NE 68105 **Effect of chronic levodopa on vitamin B6 metabolism in discrete regions of rat brain.** Pharmacologist. 19(2):226, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effect of chronic levodopa administration on vitamin B6 metabolism in discrete regions of rat brain was reported. The animals were given levodopa daily and various brain areas were assayed for pyridoxal phosphate (PLP) and pydiodoxal kinase (PL-kinase); in addition, the dopamine (DA) levels in the basal banglia were determined. Control levels of PLP were highest in inferior colliculus and lowest in spinal cord, while the control activity of PL-kinase was highest in olfactory bulb and lowest in spinal cord. Levodopa increased the activity of PL-kinase in basal ganglia, followed by a gradual, nonuniform return to basal level. The initial elevation of PL-kinase may be due to adaptive responses caused by increased DA formation. It is suggested that the levodopa induced alteration in the activity of PL-kinase modifying the synthesis of PLP may be responsible

for fluctuations in the therapeutic effectiveness of levodopa and also for the drug's chronic toxicity. (Author abstract modified)

001106 Eccles, R.; MacLean, A. G. Dept. of Physiology, University College, Cardiff CF1 1XL, Wales **Relaxation of smooth muscle following contraction elicited by sympathetic nerve stimulation in vivo.** British Journal of Pharmacology (London). 61(4):551-558, 1977.

The relationship between response amplitude and rate of recovery was investigated by analyzing the effects of phenoxybenzamine, desmethylimipramine, and cocaine upon responses to nerve stimulation. Administration of desmethylimipramine or cocaine caused increases in both the amplitude and duration of the nasal and membrane responses which may be explained by inhibition of neuronal uptake of noradrenaline. Phenoxybenzamine depressed the responses to nerve stimulation, but had little effect on the relationship between response amplitude and rate of recovery. Because the intial rate of recovery is independent of response amplitude and complicating factors such as biphasic recovery curves, it is suggested that the graphs of rate of recovery against amplitude of responses can provide information about the process of neuroeffector transmission. 33 references. (Author abstract modified)

001107 Edvinsson, L.; Hardebo, J. E.; Harper, A. M.; McCulloch, J.; Owman, Ch. University of Lund, Lund, Sweden **Action of dopamine agonists on brain vessels in vitro and after in vivo microapplication.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):350-351, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, the direct cerebrovascular action of dopaminergic agents on brain vessels was studied by a combination of in vitro and in vivo methods. During in vitro conditions the relaxed middle cerebral artery of the cat constricted in response to epinine, apomorphine, dopamine, and the dopamine receptor agonist ET-495; these effects were counteracted by phenoxybenzamine, phentolamine, and methysergide, but not by haloperidol. The vasomotor effect in vivo of dopamine agents was analyzed in applying apomorphine on individual pial arterioles of anesthetized cats, resulting in dilation independent of the resting vessel caliber. Results demonstrated that the cerebral vessels can respond directly to dopamine receptor agonists and that the response correlates well with effects observed on cerebral blood flow. 3 references.

001108 Ehara, Takashi; Mitsunobu, Katsusuke; Kuroda, Shigetoshi; Ohshimo, Toshinori; Nagao, Tadao; Otsuki, Saburo. Department of Neuropsychiatry, Okayama University, Japan **Brain distribution of lithium and indole amine metabolism in dogs after chronic lithium administration.** Psychiatria et Neurologia Japonica (Tokyo). 79(4):205, 1977.

At the 26th Central Japan Shikoku Symposium of Neuropsychiatrists, November 1976, Okayama, Japan, the results of brain examination of four dogs who were given chronic lithium mixed with their food are reported. Measurements were made of brain concentrations of lithium, 5-hydroxytryptamine, and 5-hydroxyindoleacetic acid concentrations. Administration of the lithium was between 39 and 77 days with intoxication of between 10 and 48 days. The dogs died at dosages between 100 and 139mg/kg. Lithium was measured by the Bond method. There were differences in the lithium distribution in the brain with the tonsillar nucleus, the thalamus, and hippocampus. There was an overall tendency for concentrations of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid to be low.

001109 Eidelman, B. H.; Mendelow, A. D.; McCalden, T. A.; Bloom, D. Department of Physiology, University of the Witwatersrand Medical School, Johannesburg, South Africa **Lipoprotein potentiation of the cerebrovascular response to intra-arterial 5-hydroxytryptamine.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):78-79, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, the interaction between 5-hydroxytryptamine (5-HT) and plasma beta-lipoproteins in relation to a possible potentiating effect of the latter on the cerebral vasoconstrictor effect of 5-HT was reported in 16 baboons. The cerebrovascular response to intraarterial infusion of 5-HT only and to infusion of 5-HT accompanied by simultaneous infusion of beta-lipoprotein concentrate was observed. The infusion of 5-HT only produced no significant change in cerebral grey matter flow, but the mean resting grey matter flow during beta-lipoprotein infusion was significantly higher. Administration of 5-HT with beta-lipoproteins significantly decreased grey matter flow compared to baseline beta-lipoprotein and 5-HT values. Results confirmed that intraarterial administration of 5-HT does not cause significant change in grey matter flow, but beta-lipoprotein appears to sensitize the cerebral vasculature to intraarterial 5-HT which then produces constriction by unknown mechanisms. 10 references.

001110 Eisenberg, R. M.; Sparber, S. B. University of Minnesota at Duluth, School of Medicine, Duluth, MN 55812 **Effects of naloxone following a single administration of levorphanol tartrate in the naive rat.** Pharmacologist. 19(2):141, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a series of studies of the effects of naloxone on plasma corticosterone levels following a single administration of levorphanol tartrate (LT) to naive rats was reported. LT alone increased plasma corticosterone in previously untreated animals in a dose related fashion. Plasma corticosterone returned to preinjection values within 2 hr. Naloxone, injected i.v. after the single dose of LT, produced a similar elevation in plasma corticosterone; this effect was not seen in animals which had not received LT. It is suggested that the naloxone induced increase in plasma corticosterone may be a response to physical stress associated with the reversal of the physiological effects produced by LT. (Author abstract modified)

001111 El-hawari, A. M.; Cianflone, D.; Sharkawi, M. University of Montreal, P.Q., Canada **Effects of disulfiram on pharmacological activity, toxicity and fate of morphine in rats.** Pharmacologist. 19(2):142, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of disulfiram on the pharmacological effects, toxicity, and fate of morphine in rats was reported. Disulfiram, administered prior to morphine, enhanced morphine analgesia and catalepsy. Morphine toxicity was also increased by pretreatment with disulfiram. In disulfiram treated animals, plasma concentrations and half-lives of morphine and morphine metabolites were higher than in controls. Three hours after administration of radiolabeled morphine to disulfiram pretreated rats, total

radioactivity excreted in bile and in urine was lower, radioactivity present in liver and kidney was significantly increased, and brain radioactivity was slightly increased as compared to controls. Rats without bile cannula excreted less radioactivity during 48 hr after disulfiram pretreatment. N-demethylation of morphine by liver microsomes was considerably inhibited after disulfiram, but glucorinidation was slightly increased. It is suggested that the enhancement of morphine activity and toxicity after disulfiram may result from changes in morphine metabolism and dispo sition. (Author abstract modified)

001112 Elliott, P. N. C.; Jenner, P.; Chadwick, D.; Reynolds, E.; Marsden, C. D. King's College Hospital Medical School, Denmark Hill, London SE5, England **The effect of diphenylhydantoin on central catecholamine containing neuronal systems.** Journal of Pharmacy and Pharmacology (London). 29(1):41-43, 1977.

Since diphenylhydantoin causes dyskinesias resembling those produced by antipsychotic drugs, the effect of diphenylhydantoin on central dopaminergic and noradrenergic systems was studied in male Wistar rats. Diphenylhydantoin produced dose dependent inhibition of circling behavior induced by apomorphine and amphetamine. There was 52% reduction in dopamine levels on the lesioned side, but no change in norepinephrine or serotonin concentrations. Unilateral intrastriatal administration of diphenylhydantoin followed by apomorphine s.c. produced ipsiversive turning, while saline plus apomorphine had no effect. Diphenylhydantoin did not affect apomorphine induced reversal of reserpine akinesia or apomorphine induced stereotypy. Diphenylhydantoin had no effect on homovanillic acid or dihydroxyphenylacetic acid concentrations in the striatal or mesolimbic areas when given to mice 1 to 2 1/2 hr before death and did not alter the decrease in dopamine concentration induced by alpha-methyl-p-tyrosine. It is concluded that diphenylhydantoin does seem to have some effect on cerebral dopamine systems, but the nature of this interaction is complex. 25 references.

001113 Enero, Maria A. Inst. de Invest. Farm., Consejo Nacional de Investigaciones Cientificas y Tecnicas, Junin 956, 5 Piso, (1113) Buenos Aires, Argentina **Properties of the peripheral opiate receptors in the cat nicitating membrane.** European Journal of Pharmacology (Amsterdam). 45(4):349-356, 1977.

In a study of the properties of the peripheral opiate receptors in the cat nictitating membrane, the noradrenaline overflow and the contractile response elicited by nerve stimulation of the muscle were inhibited by 1 microM morphine in the cat nictitating membrane. This concentration of morphine did not modify the response of the muscle to exogenous noradrenaline. The inhibitory effect of morphine was increased by low Na+(50mM), whereas the capacity of naloxone as antagonist to morphine was higher with 150mM than with 50mM Na+. These results suggest that the peripheral opiate receptors which interact with noradrenergic neurotransmission could show a sodium allosteric transformation similar to that described for the brain opiate receptor. The effect of morphine was enhanced by manganese ion in the presence of normal Na+. It is postulated that the affinity of the ligands for presynaptic receptors which regulate adrenergic neurotransmission might be modified during the physiological changes in ion concentration which accompany nerve depolarization. 23 references. (Author abstract modified)

001114 Euvrard, Catherine; Javoy, France; Herbet, Alain; Glowinski, Jacques. Laboratoire de Neurophysiologie, College de France, 11, place Marcellin Berthelot, F-75321 Paris Cedex 05, France **Effect of quipazine, a serotonin-like drug, on striatal cholinergic interneurones.** European Journal of Pharmacology (Amsterdam). 41(3):281-289, 1977.

The effect of quipazine, a serotonin like drug, on striatal cholinergic neurons was studied in male Charles River rats. Quipazine i.p. increased acetylcholine levels in the striatum after 1 hr, but not in the hippocampus or in the parietal cortex. Quipazine, 10mcM in vitro or 30mg/kg i.p. in vivo, did not affect the activities of choline acetyltransferase or cholinesterase. Destruction of dopaminergic neurons by 6-hydroxydopamine had no effect on acetycholine levels before quipazine, but after 30mg/kg quipazine i.p.,acetycholine levels in the striatum decreased about 40% after 1 hr. Para-chlorophenylalanine 48 hr and 24 hr before sacrifice depleted serotonin stores, but had no effect on acetylcholine levels. When quipazine was given to rats pretreated with para-chlorophenylalanine, acetylcholine levels were increased 18%, compared with a 39% increase in saline pretreated rats. Administration of 5-hydroxytryptophan, Lilly 110140, or chlorimipramine did not affect striatal acetylcholine levels, but 5-methoxy-N,N-dimethyltryptamine increased acetylcholine after 30 min. Thus, serotonergic neurons projecting to the striatum seem to inhibit cholinergic neurons there. 40 references.

001115 Evans, David B.; Liu, Shean-jang; Wang, Richard I. H. Wood Veterans Administration Center, Wood, WI **Interaction of amitriptyline and morphine in morphine tolerant and nontolerant rats.** Pharmacologist. 19(2):170, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of amitriptyline (AT) on the analgesic action and distribution of morphine (M) in M tolerant rats and nontolerant rats was reported. The animals were rendered tolerant to M analgesia by subcutaneous implantation of a pellet. AT given 1 hr prior to M in nontolerant rats caused an increase in the intensity and the duration of M analgesia as determined by the hot plate method. No differences in total levels or in the morphine/morphine glucuronide (M/MG) ratio in brain, liver, or urine were detected 30 min, 60 min, or 90 min after administration of radiolabeled M. Administration of AT 1 hr prior to M in tolerant rats caused a similar increase in M analgesia. However, the brain levels of radiolabeled M at 60 min after administration were lower in AT pretreated animals than in controls. Distribution of radioactivity in tolerant rats showed no significant change in the total radioactivity or the M/MG ratio in urine or liver. It is suggested that AT potentiation of M analgesia may be due to a pharmacodynamic rather than a pharmacokinetic interaction. (Author abstract modified)

001116 Evans, Richard H.; Francis, Alison A.; Watkins, Jeffrey C. Dept. of Pharmacology, Medical School, University of Bristol, University Walk, Bristol BS8 1TD, England **Differential antagonism by chlorpromazine and diazepam of frog motoneurone depolarization induced by glutamate-related amino acids.** European Journal of Pharmacology (Amsterdam). 44(4):325-330, 1977.

The effects of some central depressant drugs on amino acid induced depolarization of motoneurons have been determined in the isolated hemisected frog spinal cord. Chlorpromazine and diazepam produced a similar differential pattern of depression of amino acid induced depolarizations. Responses induced by L-homocysteate were markedly antagonized by these drugs, while responses to quisqualate were unaffected. L-

Aspartate induced responses were antagonized more than L-glutamate induced responses. This pattern of antagonism resembles that previously described for Mg2+. In contrast, pentobarbital and the inhibitory amino acids GABA and beta-alanine depressed amino acid induced responses in a more uniform manner. The differential effects observed with chlorpromazine and diazepam provide further support for the possibility that responses to excitant amino acids structurally related to L-glutamate may have different underlying mechanism. 12 references. (Author abstract modified)

001117 Farah, M. B.; Adler-Graschinsky, E.; Langer, S. Z. Consejo Nacional de Investigaciones Cientificas y Tecnicas, Junin 956-5 Piso, (1113), Buenos Aires, Argentina **Possible physiological significance of the initial step in the catabolism of noradrenaline in the central nervous system of the rat.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 297(2):119-131, 1977.

The hypothalamus, cerebral cortex, and cerebellar cortex of rat brain were labeled in vitro with 3H-noradrenaline (3H-NA), and the metabolism of the tritiated transmitter was studied during spontaneous outflow and under conditions of release elicited by exposure to 20mM K plus. In these three areas of the rat CNS, 3H-NA accounted for about 40% of the total radio activity in spontaneous outflow, while the 3H-O-methylated deaminated 3H-OMDA fraction and 3H-3-4-dihydroxyphenylglycol (3H-DOPEG) were the main metabolites. Exposure to a reserpine type agent induced a selective increase in spontaneous outflow of the 3H-DOPEG, while contribution of 3H-OMDA metabolites to the increase was very small. Results were compatible with the view that formation of the deamined glycol is the first step in 3H-NA metabolism in the rat CNS. Determination of some NA metabolites levels retained in the CNS does not necessarily represent an accurate reflection of central noradrenergic activity or of selective metabolic pathways. It is therefore important to take into account the transmitters and their metabolities in the tissue, as well as outflow from the structures studied under in vivo or in vitro conditions. 43 references. (Author abstract modified)

001118 Farah, M. B.; Patil, P. N.; Langer, S. Z. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Evidence for an alpha-adrenoceptor mediated control of norepinephrine (NE) release induced by depolarization with potassium in the central and peripheral nervous systems of the rat.** Pharmacologist. 19(2):226, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the possible involvement of alpha-adrenergic receptors in the control of norepinephrine (NE) release induced by depolarization with potassium (K) in the central and peripheral nervous systems of the rat was reported. Tissue slices of hypothalamus and cerebral cortex were incubated with radiolabeled NE and the effects of phenoxybenzamine (PBA), clonidine (Cl), and cocaine on the release of radioactivity induced by exposure to K were determined. In hypothalamus, PBA induced a dose dependent increase in release of radioactivity induced by K, while Cl decreased the K induced overflow. Similar results were obtained in cortex. Pretreatment with Cl before and during exposure to PBA prevented the increase observed after exposure to PBA alone. Cocaine had no significant effect on release of radioactivity. PBA also increased the release of radioactivity induced by exposure to K from slices of vasa deferentia. In both systems, exogenous NE depressed radioactivity release induced by exposure to K in a dose dependent manner. It is concluded that alpha-adrenoceptors are involved in regulating NE release evoked by sustained depolarization (high K) of the nerve membrane. (Author abstract modified)

001119 Ferris, R. M.; Tang, F. L. M. Wellcome Research Laboratories, Research Triangle Park, NC **Influence of isomers of amphetamine, deoxypipradiol, and methylphenidate on uptake and release of 3H-catecholamines in synaptic vesicles of rat brain.** Pharmacologist. 19(2):240, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of isomers of amphetamine, deoxypipradrol, and methylphenidate on the uptake and release of radiolabeled catecholamines in rat brain synaptic vesicles was reported. The adenosine triphosphate/magnesium dependent uptake of radiolabeled dopamine (DA) and radiolabeled norepinephrine (NE) into synaptic vesicles was inhibited more effectively by dextroamphetamine than by levoamphetamine. Neither isomer at concentrations equivalent to their IC-50 values produced a significant effect on the release of DA or NE. However, at concentrations 3 times to 10 times their IC-50 values, both isomers significantly increased the release of DA but not NE from synaptic vesicles. In contrast, dextrodeoxypipradrol and its levorotatory isomer were approximately equipotent inhibitors of radiolabeled catecholamine uptake into synaptic vesicles. The 1R:2R isomer of methylphenidate was twice as potent as its 1R:2R isomer as an inhibitor of uptake of radiolabeled DA and NE. None of the isomers of deoxypipradrol and methylphenidate influenced release of catecholamines at concentrations 3 times to 10 times higher than their IC-50 values as inhibitors of uptake. It is suggested that the amine pump present in synaptic vesicles is sensitive to the stereochemical configuration around the alpha carbon of amphetamine but is not sensitive to the stereochemical configuration around the analogous carbon of methylphenidate or deoxypipradrol. These observations are opposite to those for the amine pump present in neuronal membranes. (Author abstract modified)

001120 Fertziger, Allen P.; Fischer, Roland. Dept. of Pharmacology, George Washington University Medical Center, Washington, DC **Interaction between narcotic antagonist (naloxone) and lysergic acid diethylamide (LSD) in the rat.** Psychopharmacology (Berlin). 54(3):313-314, 1977.

In a study to examine any possible antagonist interaction between lysergic acid diethylamide (LSD) and the narcotic antagonist naloxone, LSD administration in rats elicited a diphasic reaction consisting of a brief excitable period (up to 8 min) followed by a prolonged catalepsy (8 min to 1 h). While the cataleptic response was antagonized by a single injection of naloxone (given 30 min after LSD administration), pretreatment with naloxone shortened the excitable phase and potentiated the catalepsy. These results are compatible with the notion that LSD may set free analgesic endorphins (enkephalins), the latter of which are known to be counteracted by naloxone. Naloxone may counteract LSD induced analgesia in humans. 15 references. (Author abstract modified)

001121 File, Sandra; Hyde, J. R. G. Department of Pharmacology, School of Pharmacy, University of London, Brunswick Square, London WC1N 1AX, England **The effects of p-chlorophenylalanine and ethanolamine-O-sulphate in an animal test of anxiety.** Journal of Pharmacy and Pharmacology (London). 29(12):735-738, 1977.

To examine the role of 5-hydroxtryptamine (5-HT) and gamma-aminobutyric acid (GABA) in anxiety reduction, the effects of p-chlorophenylalanine and ethanolamine-O-sulphate were studied using a newly developed animal test which measures active social interaction between male rat pairs. Analysis of data indicates that p-chlorophenylalanine has effects qualitatively similar to those previously found with chronic chlordiazepoxide and with acute ethanol in the social interaction test of anxiety. This result is compatible with the idea that a reduced turnover of 5-HT is important in anxiety reduction. On the same test, ethanolamine-O-sulphate, which raises brain GABA, was without effect, suggesting raised concentrations of this acid are not essential for anxiety reduction. 18 references. (Author abstract modified)

001122 Fjalland, B.; Boeck, V. Department of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Copenhagen, Denmark **Neuroleptic influence on various neurotransmitter substances.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):47, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the antagonistic effect of neuroleptics (thiozanthenes, phenothiazines, butyropheonones, and clozapine) against acetylcholine, histamine (HIS), 5-hydroxytryptamine (5-HT) and noradrenaline (NA) was examined in in vivo and in vitro models and compared to the effect on dopamine (DA) stimulated adenylate cyclase and gamma-aminobutyric acid (GABA) uptake. Piflutixol and ciz(Z)-flupenthixol had high affinity to DA and NA receptors, but weak affinity for muscarinic (MUS) receptors. Clozapine and cis(Z)-chlorprothixene had high affinity for MUS, HIS, and 5-HT receptors, but the DA and NA receptor affinity was low when compared to piflutixol. Fluphenazine had higher affinity for the DA than the other receptors, whereas haloperidol had low affinity for all receptors when compared to the other neuroleptics. The uptake of GABA was inhibited by all neuroleptics, but in rather high concentrations. The data indicate that neuroleptic compounds possess very different profiles with respect to interaction with neurotransmitter substances.

001123 Frankel, D.; Khanna, J. M.; LeBlanc, A. E.; Kalant, H. Dept. of Pharmacology, University of Toronto, Toronto, Ontario M5S 2S1, Canada **Effect of p-chlorophenylalanine on development of cross-tolerance between pentobarbital and ethanol.** Canadian Journal of Physiology and Pharmacology (Ottawa). 55(4):954-957, 1977.

The effect of p-chlorophenylalanine (p-CPA) on tolerance development to ethanol in rats which were chronically treated with pentobarbital is studied to examine cross-tolerance development between ethanol and pentobarbital. Rats developed cross-tolerance to the motor impairing effects of ethanol after daily oral administration of pentobarbital. Chronic administration of p-CPA, in a dosage regimen previously demonstrated to maintain extensive brain serotonin (5-HT) depletion, slowed down cross-tolerance development. p-CPA did not appear to exert this effect by altering the disposition of ethanol, since blood ethanol levels measured 20 min after ethanol administration were not affected by p-CPA treatment. This study extends previous findings with respect to the inhibitory effects of p-CPA on tolerance development to ethanol and pentobarbital, and suggests that 5-HT may play a role in cross-tolerance development between ethanol and pentobarbital. 14 references. (Author abstract modified)

001124 Frederickson, Robert C. A.; Burgis, Vigo; Edwards, J. David. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46206 **Hyperalgesia induced by naloxone follows diurnal rhythm in responsivity to painful stimuli.** Science. 198(4318):756-758, 1977.

Observations of a diurnal rhythm in the responsiveness of mice to nociceptive stimuli and in the hyperalgesic activity of naloxone are presented. The studies employed Cox standard 5-week-old mice that were raised and maintained on a specified lighting schedule and either had continued access to food and water or were deprived for 2 to 6 hours before testing. It is concluded that the observed rhythms may follow a diurnal rhythmicity in the activity of endogenous opioid peptides and may partly account for previous controversy over the direct action of naloxone in opiate naive animals. 18 references.

001125 Frye, Gerald Dalton. University of Carolina, Chapel Hill, NC **Studies of a pharmacological model of ethanol dependence in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-27250 HC$15.00 MF$8.50 219 p.

Ethanol dependence in the rat was studied in the framework of a model characterized by: 1) the absence of nutritional deficiency, illness, nonethanol drug toxicity, or adverse environmental effects; 2) maintenance of chronic ethanol intoxication as indicated by behavioral and blood ethanol concentration measures; and 3) the demonstration of tolerance and physical dependence upon withdrawal. The involvement of norepinephrine (NE), dopamine (DA), and 5-hydroxytryptamine (5-HT) in development of physical dependence and withdrawal and the actions of thyrotropin releasing hormone (TRH), apomorphine (AM), and desmethylimipramine (DMI) in antagonizing ethanol effects were also studied. Ss were fed ethanol liquid diets. Ethanol removal resulted in elimination from blood after 4 to 6 hrs and spontaneous withdrawal reactions beginning at 2 to 3 hrs and lasting as long as 96 hrs. Incidence and severity of spontaneous and audiogenically induced withdrawal signs were directly related to ethanol exposure level. Long-term depletion of NE, DA, both NE and DA, or 5-HT did not alter development of physical dependence, but AM and DMI reduced manifestations of withdrawal susceptibility. None of the tested antagonists specifically antagonized either ethanol induced depression or withdrawal hyperexcitability. It is concluded that this model, although it does not include purely voluntary ethanol selection, can be used to study pharmacological mechanisms involved in ethanol dependence. (Journal abstract modified)

001126 Fuentes, J. A.; Garzon, J.; Del Rio, J. Institute of Medicinal Chemistry, National Center for Organic Chemistry, C.S.I.C., Juan de la Cierva, 3, Madrid-6, Spain **Potentiation of morphine analgesia in mice after inhibition of brain type B monoamine oxidase.** Neuropharmacology (Oxford). 16(12):857-862, 1977.

Experiments were undertaken in mice to determine whether morphine analgesia could be differentially affected by selective inhibition of A or B forms of monoamine oxidase (MAO) and to detect possible correlations between analgesic effect and morphine concentrations in the brain. Morphine analgesia in mice was significantly potentiated by deprenyl and pargyline, selective inhibitors of brain type B MAO. Clorgyline and Lilly 51641, selective inhibitors of type A MAO, did not modify the morphine effect. Morphine analgesia was also potentiated by increasing the dose of Lilly 51641 so as to block type B MAO by about 70%, or by inhibiting unspecifically both enzyme forms after either tranylcypromine or high doses of pargyline. No general correlation was found between an increased brain concentration of morphine and the enhance-

ment of morphine analgesia induced by some of the MAO inhibitors tested. 2-Phenylethylamine, a specific substrate of type B MAO, was also found to potentiate morphine analgesia. It is suggested that endogenous substrates of type B MAO may modulate the opiate receptor binding. 36 references. (Author abstract modified)

001127 Gal, E. M.; Sherman, A. D. Neurochemical Research Labs., Dept. of Psychiatry, University of Iowa, Iowa City, IA 52242 **Metabolism of fenfluramine to m-trifluoromethylbenzoylglycine in rat brain.** Communications in Psychopharmacology. 1(4):353-361, 1977.

A novel detoxication pathway for the brain is demonstrated. The biosynthesis of hippuric acid has been described only for mammalian liver and kidney. Upon intraventricular administration of fenfluramine, one of the cerebral metabolites was identified as m-trifluoromethylbenzoylglycine (FE2). Intraperitoneally administered fenfluramine did not result in the appearance of FE2 in the brain. Studies in vitro also confirmed the synthesis of this compound and hippuric acid from m-trifluoromethylbenzoic or benzoic acid with glycine by a 12,000 x g supernatant of rat brain. m-Trifluoromethylbenzoylglycine obtained from brain proved to be isochromatographic in various systems with a mass spectrographically pure synthetic sample. 7 references. (Author abstract)

001128 Garcin, Francoise; Coyle, Joseph T. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Effects of perinatal 6-hydroxydopamine treatment on opiate receptor distribution in adult brain.** Communications in Psychopharmacology. 1(3):283-290, 1977.

Effects of perinatal 6-hydroxydopamine treatment on opiate receptor distribution in the adult rat brain were studied. Peripheral treatment of newborn rats with 6-hydroxydopamine altered the levels of norepinephrine, with a severe reduction in the cerebral cortex and increases in the medulla pons, locus coeruleus and cerebellum. Results indicate that in the treated rats, opiate receptor binding is significantly increased in the locus coeruleus and the cerebellum, two areas in which hyperplasia of noradrenergic processes has occurred. It is surmised that ontogenetic factors may significantly influence the action of opiates and endorphins in mature central nervous system. 17 references. (Journal abstract modified)

001129 Gardiner, T. H.; Lewis, J. M.; Shore, P. A. University of Texas Southwestern Medical School, Dallas, TX 75235 **Distribution of clozapine in the rat: evidence for active transport in lung.** Pharmacologist. 19(2):168, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the distribution of clozapine in the rat was reported. A fluorometric procedure for the estimation of the drug was devised and the drug was measured in various tissues after intraperitoneal injection. In a 24 hr urine collection, less than 1% of the injected drug was found. After 1 hr, clozapine concentrations were greatest in lung, spleen, liver, and brain while concentrations in heart, kidney, skeletal muscle, blood, and fat were insignificant. After 6 hr, clozapine levels in lung remained high whereas concentrations in all other tissues had declined to very low levels. When rat lung slices were incubated in the presence of oxygen in clozapine solution, the drug was taken up by the tissue against a concentration gradient, attaining a maximum tissue/medium (T/M) ratio of 97 after 4 hr. When concentration of the drug was raised 10 fold, the 1 hr T/M ratio declined to 21. Chlordiazepoxide, amphetamine, and morphine depressed the 1 hr T/M ratio of clozapine by up to 50%. Clozapine uptake was also decreased 19% by anerobic conditions and 25% by the presence of 2,4-dinitrophenol. It is suggested that the lungs are a site of active transport and accumulation of clozapine and perhaps other drugs. (Author abstract modified)

001130 Gehrmann, John E.; Havstad, James W.; Killiam, Keith F., Jr. Department of Pharmacology, University of California at Davis School of Medicine, Davis, CA 95616 **Spectral analysis of the differing EEG effects of benzodiazepines, meprobamate, glutethimide and amobarbital in Macaca mulatta.** Pharmacologist. 19(2):155, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the differential effects of benzodiazepines, meprobamate, glutethimide, and amobarbital on the electroencephalogram (EEG) in Macaca mulatta was reported. All agents produced increases in total spectral power but could be differentiated on the basis of the frequency bands within the averaged spectra reflecting the greatest change. Benzodiazepines produced less increase in spectral power but showed greater temporal fluctuation in certain bands in the postdrug state. It is suggested that further distinctions among the benzodiazepines based on differences in temporal stability of spectral density might be related to the degree of behavioral depression following drug administration. (Author abstract modified)

001131 Geisler, A.; Klysner, R. Department of Pharmacology, University of Copenhagen, DK-2100 Copenhagen, Denmark **Combined effect of lithium and flupenthixol on striatal adenylate cyclase.** Lancet (London). No. 8008:430-431, 1977.

In a letter to the editor, the effect of lithium and alpha-flupenthixol on striatal adenylate cyclase activity in the rat was studied. Both lithium and flupenthixol inhibited rat striatal adenylate cyclase activated maximally by dopamine, inhibition being 29% for either 10mM/l lithium or 50nM/l alpha-flupenthixol. For the combined addition of the two drugs, the inhibition was 64%. Neither drug had any effect on basal adenylate cyclase activity. It is suggested that adverse human reaction to combined lithium/neuroleptic treatment may be related to this combined inhibition of adenylate cyclase in the striatum. 12 references.

001132 Geller, E. B.; Durlofsky, L.; Harakal, C.; Cowan, A.; Adler, M. W. Temple University School of Medicine, Philadelphia, PA 19140 **Pentobarbital does not influence the antinociceptive effects of morphine in naive or morphine-tolerant rats.** Pharmacologist. 19(2):142, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effect of sodium pentobarbital on the antinociceptive effects of morphine in rats was reported. Pentobarbital alone had neither antinociceptive nor hyperalgesic properties. In naive rats, the dose/response line for morphine antinociception as measured by the tail compression test was not displaced by pretreatment with pentobarbital. Similarly, in morphine tolerant rats, pentobarbital had no significant influence on the morphine dose/response line. It is concluded that pentobarbital does not modify the antinociceptive effects of morphine in the rat tail compression test. (Author abstract modified)

001133 Ghosh, P. K.; Hrdina, P. D. Dept. of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Ont. K1N

9A9, Canada **Effects of tricyclic antidepressants on the content and metabolism of dopamine in the rat striatum.** Canadian Journal of Physiology and Pharmacology (Ottawa). 55(3):383-388, 1977.

The effects of tricyclic antidepressants: imipramine (IMI), desmethylimipramine (DMI), and amitriptyline (AMI) on the levels and metabolism of dopamine (DA) in rat striatum were investigated. All three antidepressant drugs produced at 60 min a marked increase in striatal DA content. The DA enhancing effect of DMI was dose dependent until a ceiling was reached (about 140% increase). The time course study of DMI (10mg/kg) revealed a biphasic effect: an initial accumulation of DA peaking at 60 min followed by a decline in levels to about 20% of controls at 3 hr after administration. In DMI treated rats, homovanillic acid concentration was decreased to 58% at 60 min, but increased to 118% at 3 hr, whereas 3,4-dihydroxyphenylacetic acid levels were unchanged at 60 min, but significantly suppressed at 3 hr time interval. It is suggested that the observed effects of tricyclic antidepressants on striatal DA may be relevant to the beneficial effect of these compounds in Parkinson's disease. 32 references. (Author abstract)

001134 Goldberg, Alan M. Dept. of Environmental Health Sciences, Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD 21205 **Is deanol a precursor of acetylcholine?** Disease of the Nervous System. 38(12):16-20, 1977.

In a discussion of whether or not deanol acetamidobenzoate (Deaner) is a precursor of acetylcholine (ACh) the properties of the central cholinergic synapses, in terms of synthesis, localization and release are reviewed. Three possible pathways for the conversion of deanol to ACh are outlined: 1) deanol may be able to directly be converted into choline by a transmethylation; 2) deanol may be itself acetylated, resulting in acetyldeanol; or 3) deanol may by phosphorylated to deanol phosphate, then methylated to choline phosphate. 34 references.

001135 Goldman, Harold; Murphy, Sharon. Wayne State University School of Medicine, Detroit, MI 48201 **Cerebral circulation is altered by a potent ACTH4-9 analog -- ORG 2766.** Pharmacologist. 19(2):154, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of a behaviorally potent adrenocorticotropic hormone (ACTH) 4-9 analogue (ORG 2766), which affects attentional processes and learning behavior, on cerebral blood flow in various regions of the rat brain was reported. After intravenous injection of ORG 2766 blood flow fell significantly in all areas studied except the occipital cortex of male rats. Blood flow in female rats was reduced slightly only in the frontal cortex and olfactory bulb. The data suggest that ORG 2766 produces similar metabolic effects to those of alpha-melanocyte stimulating hormone (alpha-MSH) in the brains of male rats which are reflected in similar behavioral effects. The different metabolic effects in the brains of female rats suggest that the behavioral actions of ORG 2766, and possibly those of alpha-MSH, are also likely to be different in females. It is suggested that the changes in regional circulation may be related to changes in cyclic adenosine 3',5'-monophosphate levels. (Author abstract modified)

001136 Gonzalez, Fernando A.; Byrd, Larry D. Yerkes Regional Primate Research Center, Emory University, Atlanta, GA 30322 **Physiological effects of cocaine in the squirrel monkey.** Life Sciences (Oxford). 21(10):1417-1424, 1977.

The physiological effects of cocaine in squirrel monkey (Saimiri sciureus) were investigated with attention to the cardiovascular effects of the drug. Doses of cocaine that have previously been shown to have behavioral effects produced dose related increases in arterial blood pressure, heartrate and core temperature in eight unanesthetized squirrel monkeys. The pressor effect was immediate, but heartrate increased more gradually after cocaine injection. The onset of hyperthermia was substantially delayed. It is suggested that the squirrel monkey may be a good animal model of the physiological concomitants of cocaine abuse in humans. 14 references. (Author abstract modified)

001137 Grynbaum, Alice; Kastin, Abba J.; Coy, David H.; Marks, Neville. Institute for Neurochemistry, Rockland Research Institute, Ward's Island, New York, NY 10035 **Breakdown of enkephalin and endorphin analogs by brain extracts.** Brain Research Bulletin. 2(6):479-484, 1977.

The stability of enkephalin analogs was compared to longer lipotropin sequences containing D-Ala in position 62 to determine if interactions between the N-terminal and C-terminal can account for the stability of endorphins and their marked analgesic and behavioral properties. Analogs of enkephalin containing D-amino acids in position 62, or amides in position 65, were exposed to mouse brain extracts and found to be highly resistant to breakdown. The resistance of these analogs when incubated for short periods corresponded well with their enhanced analgesic activities in vivo. After incubation for protracted periods, the analog D-Ala62, Met-NH265-LPH (61-65) was more resistant to breakdown than D-Met62, Pro-NH265-LPH(61-65) as determined by the release of N-terminal Tyr. Studies with singly substitued enkephalin analogs showed that D-Ala62 alone did not prevent aminopeptidase action but retarded the action of aminopeptidase as compared to the unsubstituted pentapeptide. The presence of D-amino acids in positions 62-65 led to the production of a tetrapeptide intermediate that was resistant to the action of carboxypeptidases. When injected intracisternally into rats, the doubly substituted enkephalin analog, D-Ala62, Met-NH265, and also D-Ala62-beta-endorphin retained analgesic potency that was reversible by naloxone. Substitution with D-Ala62 in the alpha, gamma and beta- endorphins (LPH(61-76), (61-77), and (61-91)) significantly retarded the action of brain aminopeptidases but did not prevent internal cleavages by endopeptidases. The patterns of amino acid release point to considerable differences in the susceptibility to breakdown of all three polypeptides, implying the existence of conformational restraints affecting enzymatic specificity. 9 references. (Author abstract modified)

001138 Guerrero-Munoz, F.; Cerreta, K. V.; Way, E. L. Department of Pharmacology, University of California, San Francisco, CA 94143 **Effect of acute and chronic morphine administration on synaptosomal Ca++ uptake.** Pharmacologist. 19(2):143, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of acute and chronic morphine administration to mice on the uptake of calcium ion (Ca) into brain nerve ending fractions (synaptosomes) was reported. Synaptosomes prepared from the brains of mice after acute morphine administration showed a decrease in Ca uptake. Chronic morphine treatment produced a progressive increase in the rate of Ca uptake paralleling the development of tolerance. Incubation with naloxone reversed the increase in Ca uptake by synaptosomes from tolerant mice. It is suggested that the changes in Ca permea-

bility at nerve endings produced by morphine may be related to tolerance development. (Author abstract modified)

001139 Guidotti, A.; Szmigielski, A. Lab. of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Cerebellar cGMP system: a model to study drug-receptor interaction. (Unpublished paper).** Washington, DC, NIMH, 1977. 22 p.

Rat cerebellum was used as a model tissue to study how release of known and unknown transmitters and drug receptor interaction control the synthesis of cyclic guanosine 3'-5'-monophosphate (cGMP) and the content of a protein inhibitor of protein kinases. Findings suggest that drug induced changes of cerebellar cGMP content modulate phosphorylation by altering the relationship between cGMP dependent protein kinase and content of the cerebellar inhibitor of protein kinases. It is further noted that the identification and characterization of those neuronal mechanisms which regulate cerebellar guanylate cyclase function has provided a tool for analyzing the interaction of several psychopharmacological agents (tranquilizers, analgesics, antischizophrenic and psychostimulant drugs) with the receptors which are the target for the transmitter released by climbing, mossy fiber, and GABAergic inhibitory interneurons. Experiments suggest that diazepam, as well as other tranquilizing and anticonvulsant benzodiazepines, interferes with cerebellar function by acting directly on GABA receptors, while morphine, neuroleptics, and apomorphine interfere with cerebellar cGMP system indirectly. 32 references. (Author abstract modified)

001140 Haavik, Coryce O. Department of Pharmacology, Medical College of Wisconsin, Milwaukee, WI 53233 **Profound hypothermia in mammals treated with tetrahydrocannabinols, morphine, or chlorpromazine.** Federation Proceedings. 36(12):2595-2598, 1977.

A comparison of the hypothermic action of delta9-tetrahydrocannabinol (delta9-THC) with chlorpromazine (CPZ) and morphine in mammals is examined which shows the following order of hypothermic potency: CPZ is greater than delta9-THC which is greater than morphine. A marked depression of oxygen consumption is produced by delta9-THC both in vivo and in the isolated perfused liver preparation. Simultaneous measurement of core temperature and tail temperature after delta9-THC shows that tail temperature is decreased more by delta9-THC than it is in animals that attain comparable core hypothermia without drug treatment. It is concluded that delta9-THC induced hypothermia results primarily from decreased heat production and not from increased heat loss. Therefore, the processes involved in the hypothermic response to delta9-THC appear to differ from those that mediate CPZ or morphine induced hypothermia. A hypothesis is discussed in which the hypothermic action of delta9-THC is related to inhibition of membrane ATPase. 18 references. (Author abstract modified)

001141 Halaris, Angelos E.; Freedman, Daniel X. Department of Psychiatry, University of Chicago, 950 East 59th Street, Chicago, IL 60637 **Vesicular and juxtavesicular serotonin: effects of lysergic acid diethylamide and reserpine.** Journal of Pharmacology and Experimental Therapeutics. 203(3):575-586, 1977.

An extensive analysis of subcellular serotonin (5-HT) compartmentation with and without reserpine was undertaken in order to localize further the effect of lysergic acid diethylamide (LSD) on rat brain 5-HT. The administration of LSD produced a significant increase in 5-HT in the nerve ending fraction prepared from rat whole brain. LSD caused a 50% increase in 5-HT in the vesicular fraction which was recovered after osmotic disruption of nerve endings. The increase of 5-HT in the vesicular fraction after LSD was not demonstrable in rats treated with reserpine for as long as 2 weeks postreserpine. Instead, with reserpine pretreatment the LSD induced increase in 5-HT was localized to the intrasynaptosomally derived end supernatant as early as 48 hours postreserpine. Thus, an unanticipated juxtavesicular site capable of 5-HT retention or binding was detected. In crude subcellular fractions, by contrast, significant increases in 5-HT were not observed with LSD administration until 4 days after reserpine, at which time at least a 50% 5-HT repletion had occurred. This study of drug interactions suggests a juxtavesicular compartment that may be of functional importance in presynaptic binding or transport of 5-HT. 36 references. (Author abstract modified)

001142 Hammond, D. L.; Proudfit, H. K. Department of Pharmacology, University of Illinois at the Medical Center, Chicago, IL 60612 **Potentiation of morphine analgesia by lesions of the nucleus locus coeruleus.** Pharmacologist. 19(2):140, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbis, Ohio, August 1977, a study of the role of the locus coeruleus (LC) in morphine analgesia as examined by ascertaining the effects of LC lesions on pain thresholds and morphine analgesia was reported. Bilateral lesions of the LC of rats did not alter sensitivity to pain as measured by tail flick latency. However, 2 da to 6 da after lesioning, the capacity of morphine to produce analgesia was augmented in LC lesioned rats. These observations are consistent with the hypothesis that LC cells inhibit structures thought to mediate morphine analgesia, such as the nucleus raphe magnus, nucleus raphe dorsalis, and periaqueductal gray. The relief from such inhibition by destruction of the LC is reflected in potentiation of morphine analgesia. (Author abstract modified)

001143 Harakal, C.; Tallarida, R. J.; Geller, E. B.; Maslow, J.; Adler, M. W. Temple University Medical School, Philadelphia, PA 19140 **Morphine analgesia dose-response curves in tolerant rats: modification by naloxone.** Pharmacologist. 19(2):140, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of naloxone on morphine analgesia dose response curves in tolerant rats was reported. Morphine elevated the thresholds to the noxious stimulus (tail compression) but the dose response curves were shifted to the right when compared to curves in nontolerant animals. Naloxone had no effect on the thresholds of saline treated controls, but in morphine tolerant rats pretreated with naloxone, a shift of the morphine dose response curve to the right was produced which was qualitatively and quantitatively similar to the shift obtained in nontolerant rats. The antagonistic action of naloxone in morphine tolerant animals was not significantly different from that noted in nontolerant rats. (Author abstract modified)

001144 Hashimoto, Hisakuni; Hayashi, Makoto; Nakahara, Yuzi, Niwaguchi, Tetsukichi; Ishii, Hisashi. Department of Pharmacology, Hamamatsu University School of Medicine, Hamamatsu, Japan **Actions of D-lysergic acid diethylamide (LSD) and its derivatives on 5-hydroxytryptamine receptors in the isolated uterine smooth muscle of the rat.** European Journal of Pharmacology (Amsterdam). 45(4):341-348, 1977.

Several metabolites of D-lysergic acid diethylamide (LSD) such as D-lysergic acid ethyl, 2'-hydroxyethylamide (LEO), D-lysergic acid ethyl, vinylamide (LEV), D-lysergic acid ethylamide (LAE) and D-norlysergic acid diethylamide (norLSD) are formed by liver tissue and by Streptomyces and these metabolites and synthetic N6-alkyl substituted derivatives such as N6-ethyl, N6-propyl, N6-allyl and N6-hexyl-D-norLDS (ethyl, propyl, allyl and hexyl-norLSD, respectively) were studied for their anti-s-hydroxytryptamine (anti-s-HT) and oxytoxic activities on isolated rat uteri. The LSD derivatives had less anti-5-HT activity than LSD. Except for hexyl-norLSD, N6-alkyl substituted derivatives of LSD had higher oxytocic activities than LSD, LEO or LAE. It is suggested that N6-alkyl substituted derivatives (ethyl, propyl, allyl-norLSD) have higher, but the metabolites of LSD have lower affinity for 5-HT receptors than LSD, and that N6-substituted derivatives except for hexyl-norLSD have higher intrinsic activity than LSD. 18 references. (Author abstract modified)

001145 Heikkila, Richard E.; Cabbat, Felicitas S.; Mytilineou, Catherine. Department of Neurology, Mount Sinai School of Medicine, Fifth Avenue at 100th Street, New York, NY 10029 **Studies on the capacity of mazindol and dita to act as uptake inhibitors or releasing agents for 3H-biogenic amines in rat brain tissue slices.** European Journal of Pharmacology (Amsterdam). 45(4):329-333, 1977.

The effects of the anorexic and stimulant agents mazindol and dita on 3H-biogenic amine uptake and release were determined. Mazindol and dita were very potent inhibitors of 3H-norepinephrine uptake into rat brain occipital cortex slices. Mazindol and dita were also potent inhibitors of 3H-dopamine uptake into rat neostriatal slices and of 3H-serotonin uptake into whole brain slices. Both compounds proved however to be extremely weak releasing agents for the 3H-biogenic amines in the respective brain areas. It is concluded that the effects of mazindol and dita on uptake may help to explain some of their pharmacological properties. 13 references. (Author abstract modified)

001146 Hoffman, Paula l.; Tabakoff, Boris. no address **Alterations in dopamine receptor sensitivity by chronic ethanol treatment.** Nature (London) No. 5620:551-553, 1977.

Alterations in dopamine receptor sensitivity were assessed in male mice fed a liquid diet containing 7% ethanol or an equicaloric amount of sucrose for 7 days. The test showed a tolerance to the hypothermic and behavioral effects of ethanol which continued up to 5 days after withdrawal. The maximal response of the adenylate cyclase to dopamine is decreased in ethanol tolerant animals. Although the time course of disappearance of decreased dopaminergic sensitivity seems to parallel the time course for disappearance of tolerance to ethanol, it is suggested that future studies should also evaluate the pattern of development of the alterations in dopamine receptor sensitivity in order to define the relationship of such changes in the dopaminergic systems to the development of physical dependence on ethanol. 19 references.

001147 Holbrook, Larry; Brown, Ian. Dept. of Zoology, Scarborough College, University of Toronto, West Hill, Ontario M1C 1A4, Canada **Antipsychotic drugs block LSD-induced disaggregation of brain polysomes.** Life Sciences (Oxford). 21(7):1037-1043, 1977.

The ability of antipsychotic drugs which block neurotransmitter receptor sites to inhibit LSD induced brain polysome disaggregation was investigated. Intravenous injection of LSD 10, 25 and 100 micrograms/kg to young rabbits induced brain specific disaggregation of polysomes to monosomes. Polysomes in the cerebral hemispheres, cerebellum and remaining brainstem are affected. Neurotransmitter receptors are involved since prior injection of the receptor blockers haloperidol, chlorpromazine, propranolol, phentolamine, or pizotyline prevent drug induced polysome shift. Depression of neuronal activity with sedative levels of ethanol or pentobarbital also eliminates polysome disaggregation. 75 references. (Journal abstract)

001148 Honegger, Paul; Richelson, Elliott. Department of Psychiatry, Mayo Foundation, Rochester, MN 55901 **Biochemical differentiation of aggregating cell cultures of different fetal rat brain regions.** Brain Research (Amsterdam). 133(2):329-339, 1977.

Rotation mediated aggregating cell cultures of mechanically dissociated fetal rat brains divided into three (telencephalon, mesencephalon/diencephalon and rhombencephalon), or two (telecephalon and mesencephalon/diencephalon plus rhombencephalon) parts were examined for their biochemical differentation by measuring the specific activities of choline acetyltransferase, acetylcholinesterase, glutamic acid decarboxylase, tyrosine 3-monooxygenase, aromatic L-amino acid decarboxylase, catechol methltransferase and monoamine oxidase. The results showed that such parts yielded cultures that were relatively enriched for acetylcholine synthesizing (telencephalon) or catecholamine synthesizing (mesencephalon/diencephalon and mesencephalon/diencephalon plus rhombencephalon) enzymes. In experiments to determine the effects of culture conditions on enzyme development, chronic administration of certain drugs was found to selectively influence the specific activity of certain neurotransmitter metabolizing enzymes. Thus, in cultures of whole brain, ascorbic acid decreased tyrosine 3-mono-oxygenase and aromatic L-amino acid decarboxylase while other enzymes were slightly increased; and in cultures of telencephalon and mesencephalon/diencephalon plus rhombencephalon, N6, O2-dibutyryladenosine 3',5'-cyclic phosphate decreased the specific activities of choline acetyltransferase, acetylcholinesterase, glutamic acid decarboxylase and monoamine oxidase. The results demonstrate the feasibility of growing aggregating cell cultures for pharmacological studies in developmental neurobiology. 25 references. (Author abstract modified)

001149 Hubbard, J. W.; Bailey, K.; Midha, K. K.; Cooper, J. K. Drug Research Laboratory, Health Protection Branch, Health and Welfare, Ottawa, Canada **In vivo metabolic 0-demethylation of 3,4-dimethoxyamphetamine in dog and monkey. monkey.** Pharmacologist. 19(2):163, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the metabolites formed by metabolic 0-demethylation of 3,4-dimethoxyamphetamine in the dog and monkey was reported. The metabolites were separated from urine extracts by gas/liquid chromatography (GLC) as their trifluroacetyl and monochlorodifluroacetyl derivatives. An important metabolite in both species was 3-0-methyl-alpha-methyldopamine. In the urine of monkey, 3-methoxy-4-hydroxybenzyl methyl ketone was identified, while in the urine of dog, trace amounts of alpha-methyldopamine and of 3,4-dihydroxybenzyl methyl ketone were confirmed. (Author abstract modified)

001150 Jacoby, J. H.; Poulakos, J. J. Department of Pharmacology, College of Medicine and Dentistry of New Jersey,

New Jersey Medical School, 100 Bergen Street, Newark, NJ 07103 **The actions of neuroleptic drugs and putative serotonin receptor antagonists on LSD and quipazine-induced reductions of brain 5-HIAA concentrations.** Journal of Pharmacy and Pharmacology (London). 29(12):771-773, 1977.

To examine the effects of neuroleptic drugs and putative serotonin (5-HT) receptor antagonists on lysergic acid diethylamide (LSD) and quipazine induced reductions of brain 5-hydroxyindoleacetic acid (5-HIAA), rats were pretreated with methysergide, cyproheptadine, metergoline, cinanserin, propranolol, chlorpromazine, clozapine, or haloperidol 15 min before LSD, or with quipazine plus methysergide, cyproheptadine, cinanserin, chlorpromazine, clozapine, or haloperidol. LSD reduced brain 5-HIAA concentrations. These reductions were unaffected by the 5-HT receptor antagonists, while neuroleptic compounds did alter induced 5-HIAA reductions. Haloperidol appears most effective in exerting this blockade. Similar results were obtained for these drugs when quipazine induced alterations of 5-HIAA accumulations following probenecid were studied. 32 references.

001151 James, Robert Cary. University of Utah **Amphetamine lethality in mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No.77-15355 HC$15.00 MF$8.50 66 p.

The relationship between metabolism and the triphasic dose mortality curve of mice was investigated. Findings indicated that amphetamine metabolic intermediate (MI) complexes did not affect amphetamine metabolism following inhibition of hepatic oxidative metabolism and were not involved in the mechanism whereby changes in metabolism affect mortality. Analyses of 20 to 60mg/kg doses in brain, heart, lung, and liver indicated that administration of p-hydroxyamphetamine with amphetamine did not affect mortality, and the tissue concentrations of this metabolite were not determined. Concentrations of d-amphetamine increased linearly with dose in brain and lung and nonlinearly in liver and heart. The phasic nature of d-amphetamine concentrations in heart tissue, which was elininated by SKF-525-A pretreatment, corresponded to elimination of the phasic nature of the lethal dose curve by SKF-525-A. (Journal abstract modified)

001152 Jhamandas, K.; Sawynok, J.; Sutak, M. Department of Pharmacology, Queen's University, Kingston, Ontario, Canada **Enkephalin effects on release of brain acetylcholine.** Nature (London). 269(5627):433-434, 1977.

The effects of two enkephalins, methionine enkephalin (Metenkephalin) and leucine enkephalin (Leuenkephalin) on the cortical release of acetylcholine (ACh) in Sprague-Dawley rats following intraventricular injections was studied. Results indicate that natural enkephalins may interact with opiate receptors in the brain to modulate the release of ACh from the cholinergic neurons. It was suggested that enkephalins or endorphins in the CNS may serve to modulate the release of neurotransmitters resulting from activity in the catecholaminergic and cholinergic pathways.

001153 Johansson, Barbro B.; Carlsson, Christer. Department of Neurology, Sahlgren Hospital, University of Goteborg, Goteborg, Sweden **Amphetamine-induced increase of the cerebrovascular permeability to protein.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):62-63, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, various factors theoretically of importance for the appearance of the blood-brain barrier dysfunction were reported in rats, using dye tracers as a tracer for amphetamine induced increase of cerebrovascular permeability. Rats with various CO2 tensions and pretreated with d,1-propranolol, d-propranolol, practolol, pimozid, or haloperidol were compared to controls during various mean arterial blood pressures. Extravasation and blood-brain barrier dysfunction occurred with amphetamine only (less in hyperventilated rats), pimozid, d-propranolol, and practolol, while haloperidol prevented extravasation and dysfunction and d,1-propranolol diminished the dysfunction only. Results suggested that the vasodilatory effect of amphetamine on cerebral vessels (predominantly frontoparietal cortical areas) is secondary to a catecholamine induced increase in cerebral metabolism. 5 references.

001154 Jori, A.; Dolfini, E. Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62-20157 Milan, Italy **Biochemical interaction between anorectic drugs and piribedil.** Journal of Pharmacy and Pharmacology (London). 29(9):581-582, 1977.

The effects of various anorectic drugs alone or following administration of piribedil, a dopaminergic agonist, on striatal homovanillic acid (HVA) content were studied in rats to determine whether they affect dopamine (DA) metabolism via an amphetamine like mechanism (by releasing DA from nerve endings) or a fenfluramine like mechanism (by blocking DA receptors and increasing HVA concentrations through a feedback mechanism). All of the drugs tested increased striatal HVA concentrations when given alone. Piribedil strongly counteracted the effects of fenfluramine, S-992 (trifluoromethylphenyl(benzoyloxy)ethylamino-2-propane), and SKF1-39728 (1-N-benzylmethoxy-3-trifluoromethylphenethylamine) but did not inhibit the effects of amphetamine, methylamphetamine, or mazindol. The effect of diethylpropion was reduced but not blocked by piribedil, suggesting that diethylpropion is a less potent DA agonist than amphetamine or that diethylpropion may act through more than one mechanism. It is concluded that although all of the drugs tested have the same biochemical effect on striatal HVA, they act via different mechanisms. 18 references.

001155 Kalinin, V. V. Laboratoriya neyrokhimicheskoy farmakologii, Institut farmakologii AMN SSSR, Moscow, USSR /**Effect of neuroleptics, mydanthan, and dopa on apomorphine induced stereotypy in rats.**/ Vliyanie neyroleptikov, midantana i dofa na apomorfinovuyu stereotipiyu u krys. Farmakologiya i Toksikologiya (Moskva). 40(1):16-19, 1977.

The effects of differently structured neuroleptics on apomorphine induced stereotypy in rats was investigated. Most of the known neuroleptics manifested an inhibitory effect on the stereotype. Clozapine and azabutyrone were effective only in a dose of 25mg/kg, while carbidine and promazine had no marked inhibitory effect. It is concluded that the antiapomorphine effect does not correlate with the antipsychotic activity of neuroleptics. 10 references. (Journal abstract modified)

001156 Kangas, L.; Allonen, H.; Lammintausta, R.; Pynnonen, S.; Salonen, M. Department of Pharmacology, University of Turku, Turku, Finland **Pharmacokinetics of nitrazepam in human plasma and saliva.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):56, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the pharmacokinetics of nitrazepam in human plasma and saliva were studied in human volunteers for 72 hours after administration

in tablet form. Complete absorption and a two compartment open model were assumed. The concentrations of nitrazepam in plasma and saliva were significantly correlated. The salivary concentration at 4 hours was 4% from the total plasma nitrazepam. This value was significantly lower than the protein unbound fraction in plasma at the same time; however, the protein free and cerebrospinal fluid concentrations of nitrazepam seemed to be equal.

001157 Karlen, B.; Lundgren, G.; Miyata, T.; Lundin, J.; Holmstedt, B. Division of Pharmacy, Department of Drugs, National Board of Health and Welfare, Box 607, S-751 25 Uppsala, Sweden **Effect of atropine on acetylcholine metabolism in the mouse brain.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):57, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the effect of atropine on acetylcholine (ACh) metabolism in the mouse brain was studied by following the incorporations of d6-Ch into ACh during steady state conditions and during the onset of the atropine effect. The turnover rate of ACh obtained from the formation of d6-Ch during the first 15 and 45 sec was 12.6/min/gm in the whole brain and 51.1/min/gm in striatum of mice treated with saline. It was concluded that atropine seems to act by releasing an ACh pool consisting of about 30% of the normal amount. After the new steady state is reached the turnover rate of ACh appears unchanged except in striatum, where a slight reduction is seen at the highest dose of atropine.

001158 Karoum, Farouk; Moyer-Schwing, Joan; Potkin; Steven G.; Wyatt, Richard Jed. Lab. of Clinical Psychopharm., Div. of Special Mental Health Research, IRP, NIMH, St. Elizabeths Hosp., Washington, DC 20032 **Plasma concentrations of some acidic and alcoholic metabolites derived from m- and p-tyramine, octopamine and catecholamines in humans.** Communications in Psychopharmacology. 1(4):343-352, 1977.

Mass fragmentography was employed to measure human plasma concentrations of the major acidic metabolites of m- and p-tyramine, octopamine, dopamine, epinephrine and norepinephrine. The free and conjugated forms of 3-methoxy-4-hydroxyphenylglycol (MHPG) were also measured. The means and ranges of concentrations of the acidic metabolites were comparable except for m-hydroxy-phenylacetic acid. Free, sulfate and glucuronide conjugated MHPG were also found in about equal concentrations. The method employed is considered highly reliable, and is advised for the study of plasma as a biological medium for the assessment of biogenic amine metabolism. 26 references. (Author abstract modified)

001159 Kebabian, J. W.; Calne, D. B.; Kebabian, P. R. Experimental Therapeutics Branch, NINCDS, NIH, Bethesda, MD 20014 **Lergotrile mesylate: an in vivo dopamine agonist which blocks dopamine receptors in vitro.** Communications in Psychopharmacology. 1(4):311-318, 1977.

Studies were conducted to test the possibility that the dopaminergic actions of lergotrile mesylate, an in vivo dopamine agonist, might result from the occupancy by lergotrile of the dopamine receptor regulating adenylyl cyclase activity. Lergotrile was administered to assayed portions of the caudate nucleus in male Sprague-Dawley rats and cerebellar cortex of New Zealand rabbits. It was found that lergotrile mesylate antagonizes the dopamine receptor regulating striatal adenylyl cyclase, but not the beta-adrenergic receptor regulating cerebellar adenylyl cyclase. The antagonism of the striatal dopamine receptor by lergotrile is noncompetitive with respect to dopamine. The data raise the possibility that there exist postsynaptic dopamine receptors which are not associated with adenylyl cyclase. 10 references. (Author abstract modified)

001160 Kennedy, K. A.; Hansen, A. R.; Fischer, L. J. Dept. of Pharmacology, University of Iowa, Iowa City, IA 52242 **The distribution between plasma and brain of glutethimide and 4-hydroxyglutethimide following their administration to mice.** Proceedings of the Society for Experimental Biology and Medicine. 156(3):491-495, 1977.

Possible differences in the distribution and elimination of glutethimide and its metabolite, 4-hydroxyglutethimide, in plasma and brain of mice were studied, and relationships between dose, drug levels, and pharmacological effects of the two compounds were tested. Following administration of sedative doses of d,l-glutethimide or d-4-hydroxyglutethimide to mice, the relative partition between blood and brain as well as the rate of disappearance of each substance from these tissues was found to be similar. In addition, the degree of CNS depression produced by increasing doses of either substance was directly proportional to the blood or brain level attained, indicating that the twofold greater potency of the active metabolite, relative to glutethimide, is mostly a function of its intrinsic pharmacologic activity and not dependent upon differences in drug disposition. 8 references. (Author abstract)

001161 Kennedy, L. E.; Tessel, R. E. University of Kansas, Lawrence, KS 66045 **Selectivity of 3H-biogenic amine release by d,L-amphetamine and drugs that interact with serotonergic neurons.** Pharmacologist. 19(2):195, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study comparing the potencies and efficacies with which mescaline (M), alpha-methyltryptamine (AMT), parachloroamphetamine (PCA), amphetamine (A), and fenfluramine (F) release radiolabeled norepinephrine (NE), dopamine (DA), and serotonin (5-hydroxytryptamine, 5-HT) from rat cerebral cortex was reported. A and AMT were approximately equipotent and equiefficacious in releasing each neurotransmitter and were generally the most potent of the drugs tested. For release of NE, PCA was much less potent than were A and AMT; F and M were less potent than PCA and were approximately equal in potency to each other. For release of DA, PCA was approximately as potent as A and AMT; F and M were less potent than the other drugs and were approximately equal in potency to each other. For 5-HT release, the drugs were essentially equipotent. A and AMT were most potent in releasing NE and least potent in releasing 5-HT. PCA was most potent in releasing DA and equally potent in releasing NE and 5-HT. F was equally potent in releasing 5-HT and DA and less potent in releasing NE. M released each of the neurotransmitters only at relatively high concentrations. It is suggested that: 1) the pharmacologic effects of M are probably independent of drug induced biogenic amine release; 2) the indole nucleus per se does not improve selectivity for 5-HT release; and 3) parahalogenation may improve A's selectivity for release of DA. (Author abstract modified)

001162 Khazan, Uri; Moreton, J. E. Department of Pharmacology and Toxicology, University of Maryland School of Pharmacy, Baltimore, MD 21201 **Naltrexone blockade of morphine-induced antidiuresis in the rat.** Pharmacologist. 19(2):156, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in

Columbus, Ohio, August 1977, a study of the effects of naltrexone on morphine induced antidiuresis in the rat was reported. Urine output measured at 30 min intervals after subcutaneous administration of morphine was well below control levels. Naltrexone pretreatment blocked the effects of morphine and increased the rate and total volume of urine production over control values in a dose related manner. Naltrexone administered to water loaded animals not given morphine exerted similar diuretic effects. It is suggested that naltrexone not only blocks the antidiuretic effects of morphine but has diuretic action of its own, possibly by competing with the naturally occurring morphinelike enkephalins. (Author abstract modified)

001163 King, L. J.; Minnema, K. H.; Cash, C. Dept. of Pharmacology and Psychiatry, Virginia Commonwealth University, Medical College of Virginia, Richmond, VA 23298 **Effects of acute and chronic morphine and narcotic antagonists on brain energy metabolism.** Life Sciences (Oxford). 21(10):1465-1474, 1977.

The effects of acute and chronic morphine and narcotic antagonists on brain energy metabolism in mice were investigated. Morphine sulphate (4mg/kg to 32mg/kg) produced a dose-dependent decrease in brain malate as antinociception increased. Decreased brain malate persisted 72 hours after implantation of morphine pellets by which time mice had become tolerant to antinociception. This finding suggests that malate decrease, unlike changes of other metabolites in other studies, might not be simply a result of general metabolic changes. Malate change as well as antinociception was prevented by prior injection of naloxone (3.0mg/kg) or naltrexone (0.6mg/kg) in acute experiments. Malate decrease in pelleted mice was no longer present, if withdrawal was produced by naloxone or naltrexone in mice implanted with morphine pellets for 72 hours. Brain P-creatine was elevated in all mice implanted with morphine pellets even after withdrawal, thus, apparently, representing a more generalized effect than malate change. 16 references. (Author abstract modified)

001164 Kitano, Takafumi; Takemori, A. E. University of Minnesota, Minneapolis, MN 55455 **Specific release by naloxone of 3H-morphine from superfused slices of corpus striatum of mice.** Pharmacologist. 19(2):157, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study in vitro of the accumulation of radiolabeled morphine by mouse corpus striatum tissue slices and of the effects of naloxone on morphine accumulation by these tissues was reported. The rate of morphine accumulation approached a maximum at 30 min of incubation. There appeared to be a saturable and a nonsaturable phase of accumulation when the medium concentration of morphine was varied. Tissue from morphine tolerant animals did not show uptake characteristics different from those of naive mice. The release curves of morphine by superfusion with Kreb's Ringer bicarbonate solution consisted of two components, an early rapid component and a later slower component. The release characteristics observed by superfusion was not significantly different between tissues from control and tolerant mice. Naloxone clearly produced an increase in morphine release when it was continuously superfused within 15 min after the start of the superfusion; this effect was not as apparent when naloxone was added later in the superfusion period. Slices of tissue from tolerant mice were more sensitive to the effect of naloxone than were those of control mice. The data suggest that the affinity of the corpus striatum for morphine is altered in tolerant mice. (Author abstract modified)

001165 Kitano, Takafumi; Takemori, A. E. Institute of Biological Science of Mitsui Pharmaceuticals, Inc., Chibaken, Japan **Enhanced affinity of opiate receptors for naloxone in striatal slices of morphine-dependent mice.** Research Communications in Chemical Pathology and Pharmacology. 18(2):341-351, 1977.

Enhanced affinity of opiate receptors for naloxone was demonstrated in striatal slices of morphine dependent mice. Slices of corpus striatum were allowed to accumulate 3H-morphine and then they were placed in a small chamber and superfused with Krebs-Ringer bicarbonate solution. One hundred to one pM of naloxone caused an immediate increase in the release of morphine from the slices when it was placed in the superfusion fluid at 0, 5, or 15 min after the start of the superfusion. Slices from morphine dependent mice were more sensitive to the naloxone induced release of morphine than those of control mice. It is suggested that the affinity of the opiate receptors in the corpus straitum for naloxone is increased in morphine dependent mice. 18 references. (Author abstract modified)

001166 Klaassen, Curtis D.; Iwamoto, Kikuo. University of Kansas Medical Center, Kansas City, KS 66103 **First-pass effect of nalorphine in rats.** Pharmacologist. 19(2):128, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the first pass effect of nalorphine in rats was reported. The first pass effect of the drug was measured by comparing the plasma concentration following intravenous (i.v.), oral, and intraportal administration of radiolabeled nalorphine. The route of administration did not change the quantity of drug excreted into the urine or the plasma elimination half-life (about 3 hr). In contrast, the area under the plasma concentration/time curve after oral administration or after intraportal administration was far less than that after i.v. administration. The data indicate that 83% of the oral dose was removed by extraction and/or metabolism in the intestine and/or liver during the first passage through these organs. It was estimated that approximately 60% of the overall first pass effect of nalorphine occurs in the liver and the remaining 40% in the intestine. The estimates of the relative contribution of liver and intestine in producing the first pass effect of nalorphine are consistent with the extent of hepatic uptake and intestinal glucuronidation of the drug. (Author abstract modified)

001167 Klawans, H. L.; Weiner, W. J.; Nausieda, P. A. Division of Neurology, Michael Reese Hospital and Medical Center, Chicago, IL 60616 **The effect of lithium on an animal model of tardive dyskinesia.** Progress in Neuro-Psychopharmacology (Oxford). 1(1/2):53-60, 1977.

The effects of lithium in the treatment of tardive dyskinesia was investigated using an animal model. Chronic administration of neuroleptics resulted in a decreased threshold for both amphetamine induced and apomorphine induced stereotyped behavior in guinea-pigs. This prolonged drug induced dopamine receptor site hypersensitivity was used as a model of tardive dyskinesia. Guinea-pigs treated with haloperidol alone developed a prolonged decrease in the threshold for both amphetamine induced and apomorphine induced stereotyped behavior. Those treated with haloperidol and concurrent lithium developed no alteration in threshold. The difference in the threshold in the two groups was statistically significant for both amphetamine and apomorphine. Lithium given after haloperidol induced hypersensitivity of dopamine receptors had developed had no effect on threshold for either

amphetamine or apomorphine. These results suggest that prophylactic treatment with lithium might decrease the incidence of tardive dyskinesia, but that lithium would probably be of no value in the treatment of tardive dyskinesia. 14 references. (Author abstract modified)

001168 Klee, W. A. Laboratory of General and Comparative Biochemistry, NIMH, Bethesda, MD 20014 **Some structural features governing opiate action. (Unpublished paper)** Bethesda, MD, NIMH, 1977. 1 p.

The biochemical and neurological aspects of opiate action in vivo are discussed. The role of receptor binding and occupancy is viewed as only a part of opiate mechanisms of action. Lipophilicity as measured by oil buffer partition coefficients and the mixed agonist nature of many opiates are shown to be important aspects of opiate function. It has also been demonstrated that some opiate actions are not mediated by opiate receptors. Several studies supporting these statements are reviewed.

001169 Koehn, G. L.; Karczmar, A. G. Department of Pharmacology, Loyola University Stritch School of Medicine, Maywood, IL 60153 **The behavioral effects of diisopropyl phosphofluoridate: interactions with morphine and naloxone in rats.** Pharmacologist. 19(2):141, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a series of studies in rodents of the behavioral and analgesic effects of diisopropyl phosphofluoridate (DFP), the interactions between DFP with morphine and naloxone, and the mechanism by which DFP produces its effects was reported. DFP produced analgesia and behavioral depression as measured by the hot plate, tail flick, exploratory activity, and motor activity tests. Both atropine and naloxone reversed the antinociceptive actions of DFP. At the same dose, naloxone antagonized the antinociceptive effects and the motor activity augmentation induced by morphine; however, atropine antagonized only the increased motor activity induced by morphine. DFP markedly increased serotonin (5-hydroxytryptamine) levels in several areas of rat and rabbit brains. Pretreatment with parachlorophenylalanine did not antagonize analgesia or motor activity depression produced by DFP. It is posited that DFP produces its antinociceptive and behavioral effects via the central cholinergic system and that there seems to be a relationship between the effects of morphine and cholinergic receptors. (Author abstract modified)

001170 Korsgren, G.; Sparf, B. AB Kabi, Research Department, Pharmacology, S-112 87 Stockholm, Sweden **The effect of DFP and pentobarbital on the turnover of acetylcholine in the mouse brain.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):58, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, a barbiturate, pentobarbital (PEN) and a cholinesterase inhibitor, diisopropylfluorophosphate (DFP) were compared as to their effects on the endogenous brain content of acetylcholine (ACh) and choline (Ch) and on the effects on ACh turnover. Two min after intravenous injection of PEN and DFP, the ACh concentration had increased by 50% and 90%, respectively. The increases lasted during the studies. If the drugs were injected 3 min after the injection of 3H-Ch, when 3H-ACh had reached its peak value, the half-lives of 3H-ACh were increased by 100% for both drugs while the curves for radioactive phosphorylcholine were not affected. No change in the amount of Ch was observed following PEN; however, DFP increased Ch by 40%. After 37 min 3H-Ch was significantly higher in the brain of DFP treated mice in comparison with controls; however, after PEN a significant increase in 3H-Ch was observed after 7 min.

001171 Koshakji, Richard; Ahmed, Moshira; Bush, Milton. Department of Pharmacology, Vanderbilt Medical School, Nashville, TN 37232 **Distribution and metabolism of 4'-hydroxyphenobarbital in the mouse.** Pharmacologist. 19(2):168, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the distribution and metabolism of 4'-hydroxyphenobarbital (HO-PB) in mice was reported. The half-life of HO-PB in whole blood was 15 min. The blood/brain concentration ratios were about 4 at 15 min, 1 at 20 min and 60 min, and 0.2at 2 hr. During this time period, the actual levels of drug in the brain fell from the peak values of 20 microgram/g at 15 min and 30 min to 10 micrograms/g. The proportion of very polar metabolites, possibly conjugates, in both blood and brain was 20% to 40% at all times. In the blood, liver, and kidneys, there were several other metabolites in small amounts, one of which was significantly less polar than the parent drug. The concentrations of unchanged drug in the liver and kidneys were substantially higher than those of the metabolites. (Author abstract modified)

001172 Krulik, R.; Farska, I.; Prokes, J. Psychiatric Research Unit, Med. School, Charles University, Ke Karlovu 11, Prague 2, Czechoslovakia **Effect of rubidium, lithium and cesium on brain ATPase and protein kinases.** Neuropsychobiology (Basel). 3(2-3):129-134, 1977.

The effect of rubidium, lithium and cesium on the ATPase system and 3'5'-cyclic adenosine monophosphate (cAMP) protein kinase in the brain was studied. It was demonstrated that rubidium could replace potassium in the Na+K+-ATPase system, whereas lithium and cesium had no effect on this enzyme activity in the absence of potassium. K+-dependent ATPase was activated by even low rubidium concentrations; lithium and cesium inhibited it. Neither rubidium, lithium nor cesium affected cAMP protein kinase. 15 references. (Journal abstract modified)

001173 Kuba, K.; Koketsu, K. Department of Physiology, Kurume University School of Medicine, Kurume 830, Japan **Postsynaptic potentiation of the slow muscarinic excitatory response by tetraethylammonium chloride in the bullfrog sympathetic ganglion cells.** Brain Research (Amsterdam). 137(2):381-386, 1977.

To examine the effects of tetraethylammonium (TEA) on the slow excitatory postsynaptic potential (EPSP), effects of TEA in curarized bullfrog sympathetic ganglion cells were studied on the slow acetycholine (ACh) depolarization so that the presynaptic effect of TEA could be eliminated. Results indicate that TEA potentiates the slow ACh depolarization by increasing all the components of conductance changes involved in the generation mechanism, presumably through its action on the muscarinic receptor. Further, it was shown that the slow inhibitory postsynaptic potential of Aplysia neurones, which was caused by a nonnicotinic and nonmuscarinic action of ACh, was selectively blocked by external application of TEA. 18 references.

001174 Lavretskaya, E. F.; Tat'yanenko, L. V.; Lebedeva, O. I. Nauchno-issledovatel'skiy institut po biologicheskim ispytaniyam khimicheskikh soedineniy, Moscow, USSR /Effect

of psychotropic drugs on ATPase transport of the sarcoplasmic reticulum in rabbit skeletal muscles./ Vliyanie psikhtropnykh preparatov na aktivnost' transportnoy ATF-azy sarkoplazmaticheskogo retikuluma skeletnykh myshts krolika. Farmakologiya i Toksikologiya (Moskva). 40(1):12-16, 1977.

The effects of five groups of psychotropic agents on the activity of Ca, Mg dependent ATPase of the sarcoplasmic reticulum of rabbit skeletal muscles and Ca2+ transport were investigated. Greatest inhibitory effect was exhibited by phenothiazines with piperazine ring in the side chain. Butyrophenones produced much less inhibition. Tricyclic antidepressants noticeably reduced the enzyme activity, while MAO inhibitors had little such effect. Benzodiazepine tranquilizers had moderate inhibitory effect, and trioxazine had very little effect. The stimulants caffeine, corazol, and high concentrations of lithium salts raised enzyme activity, whereas low concentrations suppressed the enzyme. 7 references. (Journal abstract modified)

001175 Lavyne, Michael H.; Koltun, Walter A.; Clement, John A.; Rosene, Douglas L.; Pickren, Kenneth S.; Zervas, Nicholas T.; Wurtman, Richard J. Harvard Medical School, Boston, MA **Decrease in neostriatal blood flow after d-amphetamine administration or electrical stimulation of the substantia nigra.** Brain Research (Amsterdam). 135(1):76-86, 1977.

To study the effect of dopamine release within the neostriatum, local blood flow was measured in the caudate nuclei and, in some cases, other areas of rat and monkey brain by the hydrogen clearance technique. Administering d-amphetamine sulfate to rats reduced caudate flow by a maximum of about 33% after 30 min; this effect could be blocked by pretreatment with haloperidol. d-Amphetamine sulfate also reduced caudate but not cortical blood flow in unanesthetized monkeys. Electrical stimulation of the pars compacta of the substantia nigra reduced ipsilateral caudate flow by about 25% without affecting flow in the contralateral caudate. This effect varied with the frequency and intensity of stimulation. These studies suggest that the intraparenchymal release of brain dopamine may modify intraparenchymal blood flow. 22 references. (Journal abstract modified)

001176 Lee, H. K.; Chai, C. Y.; Wayner, M. J.; Chung, P. M.; Cheng, J. T. Dept. of Biophysics, National Defense Medical Center, P.O. Box 8244, Taipei, Taiwan **Mechanisms of amitriptyline induced hypothermia in the rat.** Pharmacology Biochemistry & Behavior. 7(2):159-165, 1977.

The mechanism by which amitriptyline induces hypothermia was investigated in rats. The dose related hypothermia produced by amitriptyline was attenuated by phenoxybenzamine, haloperidol, diphenhydramine, atropine, and cyproheptadine, while inhibited by theophylline and by dibutyryl cyclic-adenosine-3,5-monophosphate; it was not affected by propranolol, and was strongly antagonized by pretreatment for 3 days with parachloroamphetamine. Pretreatment for 3 days with parachlorophenylalanine reduced the brain serotonin (5-hydroxytryptamine, 5-HT) concentration to 20% of the control level and completely blocked the hypothermia response to amitriptyline. The hypothermia response to amitriptyline was restored in 5-HT depleted animals following recovery of the brain 5-HT level to 50% of the control level by administration of 5-hydroxytryptophan. Intraperitoneal administration of 5-HT to 5-HT depleted animals did not increase brain 5-HT concentration or restore the amitriptyline induced hypothermia response. It is suggested that amitriptyline interacts with several transmitter substances to produce hypothermia and that 5-HT might play an important role in the mediation of amitriptyline induced hypothermia. 13 references. (Author abstract modified)

001177 Levin, M.; Diamond, B.; Havdala, H.; Borison, R. Anesthesiology Department, Mount Sinai Hospital, Chicago, IL 60608 **Clozapine and phenoxybenzamine (PBZ) alteration of central phenylethylamine (PEA) turnover.** Pharmacologist. 19(2):225, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of clozapine or phenoxybenazmine (PBZ) on central phenylethylamine (PEA) metabolism in mice was reported. Clozapine decreased PEA biosynthesis and slightly decreased PEA catabolism. PBZ increased PEA biosynthesis and catabolism. It is concluded that alpha-adrenergic receptor blockers may alter central PEA turnover. 1 reference. (Author abstract modified)

001178 Levin, R. M.; Weiss, B. Department of Pharmacology, Medical College of Pennsylvania, Philadelphia, PA 19129 **Specificity of binding of antipsychotics to the activator of cyclic nucleotide phosphodiesterase.** Pharmacologist. 19(2):203, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the binding of various drugs to the protein activator of cyclic nucleotide phosphodiesterase and of the specificity by which trifluoperazine (TFP) binds to other calcium binding proteins was reported. Antipsychotics such as TFP, chlorpromazine, penfluridol, and pimozide displayed a calcium dependent binding to the activator. Competition studies showed that these drugs competed for the same site on the protein. Agents having little or no calcium specific binding to the activator included TFP sulfoxide, promethazine, diazepam, lysergic adic diethylamide, pentobarbital, morphine, dopamine, alprenolol, theophylline, and papaverine. The antidepressants imipramine and nortriptyline showed a significant specific binding to the protein, but the binding was only 10% of that seen with TFP. Activator isolated from bovine, rat, rabbit, and human brain, and chick embryo fibroblasts, displayed similar binding to TFP. By contrast, the calcium binding proteins phospholipase A and the S 100 protein showed no specific binding to TFP, and troponin C had only 10% of the binding seen with the protein activator. It is suggested that the protein activator may be a biological receptor for antipsychotics and that the binding of drugs to this activator may provide a novel in vitro screen for new antipsychotic agents. (Author abstract modified)

001179 Light, Kim E.; Maickel, Roger P. Section on Pharmacology, Medical Science Program, Indiana University School of Medicine, Bloomington, IN 47401 **Effects of repeated dosage of tricyclic antidepressants on adipose tissue lipolytic activity in the rat.** Pharmacologist. 19(2):154, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of chronic daily subcutaneous or oral administration of several tricyclic antidepressants on the spontaneous and electrically stimulated lipolytic activity of fat pads removed from the treated rats was reported. Daily subcutaneous doses of imipramine had a continually increasing effect over 5 da to 16 da; desipramine had its most pronounced action at 5 da with lesser effect thereafter; and doxepin had a peak effect at 10 da. The response to stimulation was greatest with imipramine. Daily oral administration of amitriptyline had a maximum ef-

fect at 5 da, with lesser effects on both spontaneous and stimulated lipolysis at 10 da and 15 da, while nortriptyline and protriptyline had variable effects with duration of treatment. (Author abstract modified)

001180 Lin, S. C.; Sutherland, V. C. Department of Pharmacology, University of California, San Francisco, CA 94143 **Regional distribution of barbital in the brain of mice during the development of tolerance and physical dependence.** Research Communications in Chemical Pathology and Pharmacology. 18(2):215-231, 1977.

The development of tolerance to and dependence on barbital in mice by pellet implantation and experiments on cellular adaptation to regional distributions of barbital are described. IRC male mice each receiving a 16mg barbital pellet implanted subcutaneously for 3 days developed about 40% tolerance to barbital and more than 50% tolerance to pentobarbital as measured by sleeping time. The development of physical dependence in these mice was demonstrated by an increased sensitivity to convulsions with pentylenetetrazol. The regional specificity for the accumulation of barbital in the brain during the course of exposure to, and after withdrawal of, the drug is compared. 30 references. (Author abstract modified)

001181 Lloyd, Kenneth G.; Hornykiewicz, Oleh. Neuropharmacology Unit, Synthelabo, L.E.R.S., 31 Avenue Paul Vaillant Couturier, F-92220 Bagneux Cedex, France **Effect of chronic neuroleptic or L-DOPA administration on GABA levels in the rat substantia nigra.** Life Sciences (Oxford). 21(10):1489-1496, 1977.

To study the effects of chronic neuroleptic or L-DOPA administration on GABA levels in the rat substantia nigra, male albino rats were administered daily with haloperidol, clozapine, or L-DOPA and sacrificed 18 hours after the last dose of the drug. Acute doses of haloperidol (5mg/kg) greatly lowered nigral GABA levels, whereas after 167 daily doses the nigral GABA levels were not significantly different from controls, but were significantly increased as compared with the acutely treated animals. In contrast, acute doses of L-DOPA (2x100mg) greatly raised nigral GABA levels, whereas after chronic L-DOPA (167 days) nigral GABA levels were not significantly different from controls and were significantly lower as compared with the animals receiving the acute treatment. Clozapine (20 mg/kg) either acutely or chronically administered did not have as marked an effect on nigral GABA levels as did haloperidol. Of these various drug regimens only chronic L-DOPA significantly affected nigral glutamic acid decacarboxylase activity, producing a moderate decrease in this enzyme. 33 references. (Author abstract modified)

001182 Lokiec, Francois; Jacquot, Christian; Rapin, Jean R.; Cohen, Yves. Laboratoire de Pharmacodynamie, ERA CNRS 627, F. 92290 Chatenay-Malabry, France **Effects of amphetamine on brain biogenic amines in isolated and aggregated rats.** European Journal of Pharmacology (Amsterdam). 44(4):391-395, 1977.

An analysis of the biochemical modifications brought about by application of d-amphetamine or l-amphetamine to various noradrenergic brain areas of isolated and aggregated rats is presented. Both d and l forms of amphetamine decreased the noradrenaline levels of brain areas in isolated and in aggregated rats. d-Amphetamine decreased 5-hydroxytryptamine (5-HT) and 5-hydroxyindolacetic acid (5-HIAA) levels in aggregated rats only. l-Amphetamine induced no change in 5-HT and 5-HIAA levels. The greater sensitivity of aggregated rats to d-amphetamine can be ascribed to a change in 5-HT metabolism rather than to a modification of noradrenaline levels. 11 references. (Author abstract modified)

001183 MacGregor, T. R.; Staubus, A. E.; Morrison, B. E.; Reuning, R. Ohio State University, Columbus, OH 43210 **Plasma kinetics of naltrexone and its glucuronide in the dog.** Pharmacologist. 19(2):157, 1977.

In a paper presented at the fall meeting of the Amercian Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the plasma kinetics of naltrexone (NTX) and its glucuronide metabolite(s) (NTX-G) in dogs was reported. The NTX-G plasma level time profile over the first 60 min had a positive slope, suggestive of a formation rate from NTX greater than the elimination rate of NTX-G. In the terminal phase of the NTX-G plasma level time profile, the plasma half-life was not distinguishable from that of NTX. The area under the plasma level time curve for NTX-G was about equal to that for NTX, indicating substantial formation of NTX-G. Since the dose of NTX had been radiolabeled, plasma samples assayed for radioactivity provided a plasma level time profile for the total of NTX and its metabolites. Comparison of these total levels with the sum of NTX and NTX-G suggested the possible existence of additional metabolites in plasma. (Author abstract modified)

001184 Maggi, A.; Cattabeni, F.; Bruno, F.; Racagni, G. Institute of Pharmacology and Pharmacognosy, University of Milan, 20129 Milan, Italy **Haloperidol and clozapine: specificity of action on GABA in the nigro-striatal system.** Brain Research (Amsterdam). 133(2):382-385, 1977.

To investigate whether two antipsychotic drugs, haloperidol and clozapine, which manifest different clinical effects, act differently on brain GABAergic mechanisms in vivo, the GABA accumulation as a function time in striatum and substantia nigra was measured in rats who had been given ethanolamine-O-sulfate (EOS), EOS and haloperidol, or DOS and clozapine before sacrifice. In striatum, clozapine administered 30 minutes before killing produced an increase in the accumulation rate of GABA which was 60% greater than in animals treated only with EOS. Haloperidol, however, elicited a not significant decrease in striatum. In substantia nigra, haloperidol produced a greater increase of GABA when compared with animals treated only with EOS but clozapine decreased the accumulation rate of GABA. Haloperidol and clozapine did not change the GABA content. 19 references.

001185 Markovitz, Diane C.; Fernstrom, John D. Laboratory of Brain and Metabolism, Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Diet and uptake of aldomet by the brain: competition with natural large neutral amino acids.** Science. 197(4307):1014-1015, 1977.

Diet and uptake of aldomet by the brain was studied in rats in order to prove that aldomet competes with natural large neutral amino acids for brain uptake and that good ingestion also alters aldomet into the organ. Rats were fed regular food and the following morning were administered aldomet either alone or in combination with large amino acids, both neutral and acidic. Blood and brains were taken from the rats and analyzed fluorimetrically. Results show that there was a depression in the rise of aldomet levels in the brain of rats after injection of alpha-methylated amino acids when large neutral amino acids, but not acidic amino acids are coadministered with the drug. It is suggested that aldomet is transported into brain by the carrier for natural large neutral amino acids. 11 references. (Author abstract modified)

001186 Martin, Gregory E.; Pryzbylik, Andrew T.; Spector, N. Herbert. Merck Institute for Therapeutic Research, West Point, PA 19486 **Restraint alters the effects of morphine and heroin on core temperature in the rat.** Pharmacology Biochemistry and Behavior. 7(5):463-469, 1977.

The importance of restraint in determining the magnitude of alteration in the rat's core temperature (T) after the administration of morphine sulphate (M) and heroin hydrochloride (H) was investigated. M, in doses of 5, 15, and 30mg/kg, or H, in doses of 0.1, 1, and 5mg/kg, was administered IP to either the restrained or free moving rats as T was measured. After the administration of 5mg/kg of H or 30mg/kg of M to the restrained rat, a marked hypothermia was observed which reached a maximum mean depth of 3.1and 4.5degrees C below the baseline T, respectively. Conversely, a mean increase in T of 1.5and 1.9degrees C occurred following the administration of these same doses of M and H in the unrestrained animal. Furthermore, the hypothermic effect of the highest dose of M was not observed when the third consecutive injections of M, administered at 48 hr intervals, was administered to the restrained rat. On the other hand, when M was repeatedly administered to the free moving rat, the hyperthermic response was consistently observed. Pretreatment with naloxone hydrochloride (5mg/kg IP) effectively blocked the opiate induced hypothermia in the restrained animal, but a total dose of 10mg/kg was necessary to completely block the hyperthermic response in the free moving rat. Although the factor of restraint itself did not alter the rat's T, it did dramatically alter the action of M and H on the body temperature of the rat. 21 references. (Author abstract)

001187 Martres, M. P.; Costentin, J.; Baudry, M.; Marcais, H.; Protais, P.; Schwartz, J. C. Unite de Neurobiologie (U.109), Centre Paul Broca de l'INSERM, 2ter rue d'Alesia, F-75014 Paris, France **Long-term changes in the sensitivity of pre- and postsynaptic dopamine receptors in mouse striatum evidenced by behavioral and biochemical studies.** Brain Research (Amsterdam). 136(2):319-337, 1977.

Changes in sensitivity of striatal dopamine (DA) receptors following pharmacological treatments modifying their level of stimulation were studied in mice by measuring DA neurone activity and by biochemical and behavioral assessments of stereotyped behavior. The blockade of DA receptors induced by a single haloperidol administration resulted in hypersensitivity of presumably postsynaptic receptors and this state appeared as soon as the blockade of DA receptors was over and disappeared slowly with a half-life of about 2 days. A single dose of apomorphine led to a behavioral facilitation state characterized by increased responsiveness to the drug, possibly resulting from hyposensitivity of DA autoreceptors. This hyposensitivity of DA autoreceptors, responding to low doses of DA agonists, mediating an inhibition of DA release, and having behavioral effects opposite to those resulting from stimulation of postsynaptic receptors, may explain the behavioral facilitation. In view of its rapid appearance and long-lasting occurrence and its effect on homovanillic acid level, it is suggested that this process represents a basic neurobiological mechanism accounting for long-term increases in synaptic efficacy. The same process may play a developmental role in adverse reactions from amphetamine abuse, unwanted side-effects in levodopa therapy in Parkinsonism, and development of dyskinesias in hyperkinetic children treated with amphetamine. 48 references. (Author abstract modified)

001188 Mazurkiewicz-Kwilecki, I. M.; Bielkiewicz, B. Dept. of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Canada **Alterations in brain histamine and histidine decarboxylase activity after haloperidol and imipramine.** Progress in Neuro-Psychopharmacology (Oxford). 1(1/2):115-124, 1977.

Possible alterations in the endogenous histamine concentration and histidine decarboxylase activity in brain regions of the rat due to the administration of haloperidol and imipramine were investigated. Acute haloperidol administration in rats resulted in a significant decrease in histidine decarboxylase activity in the hypothalamus and the cortex and a slight decrease in the midbrain. Endogenous histamine concentration remained unchanged. Chronic haloperidol treatment significantly decreased hypothalamic histamine concentration, and lowered cortical histamine level. Histidine decarboxylase activity was decreased in all three brain regions. Acute treatment with imipramine resulted in significantly elevated midbrain histamine concentration and slightly increased cortical histamine. Histidine decarboxylase activity was slightly increased in the midbrain. Chronic imipramine administration caused a significant decrease in midbrain and cortical histamine concentration. Histidine decarboxylase activity was decreased in the midbrain and slightly increased in the hypothalamus. Present data indicate that histamine, the putative neurotransmitter in the brain, may play a role in the mechanism of action of neuropsychotropic drugs. 27 references. (Author abstract)

001189 McCulloch, J.; Deshmukh, V. D.; Harper, A. M. Wellcome Surgical Research Institute, University of Glasgow, Glasgow, Scotland **Indirect sympathomimetics and cerebral blood flow and metabolism.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):94-95, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, the effects of two different indirect sympathomimetics (tyramine and amphetamine) upon cerebral blood flow (CBF) and metabolism were examined in 24 anesthetized baboons. The intracarotid infusion of tyramine did not affect cerebral oxygen consumption and normocapnic CBF, although mean arterial blood pressure was elevated during infusion. Under hypercapnia conditions, tyramine reduced CBF. Intracarotid infusion of amphetamine increased CBF and cerebral oxygen consumption at a low dosage, but produced opposite results at a higher dosage. It was concluded that amphetamine affects CBF and metabolism by its ability to cross the blood-brain barrier, contrary to tyramine. 6 references.

001190 McLennan, H.; Gilfillan, Karen; Heap, Yvonne. Department of Physiology, University of British Columbia, Vancouver, B.C. IW5, Canada **Some pharmacological obervations on the analgesia induced by acupuncture in rabbits.** Pain (Amsterdam). 3(3):229-238, 1977.

To determine the physiological, neurological, and biochemical characteristics of acupuncture analgesia, a series of investigations were performed on adult rabbits. It was found that either electrical or manual agitation of the needles was necessary to the production of an analgesic effect. Development of analgesia was variable in the animals tested, and no change in pain threshold was observed in 4 of the 22 test animals. Administration of strychnine or bicuculline, inhibitory amino acid antagonists, resulted in a reversal of analgesia. Destruction of the raphe nuclei and pharmacologic procedures which interfere with trytaminergic mechanisms prevented the development of analgesia. Results suggest that the production of acupuncture analgesia probably depends upon postsynaptic

inhibition of afferent information from nociceptors, and at more than one central nervous system site. 48 references. (Author abstract modified)

001191 McMillen, B. A.; Shore, P. A. Department of Pharmacology, University of Texas Health Science Center, Dallas, TX 75235 **The relative functional availability of brain noradrenaline and dopamine storage pools.** Journal of Pharmacy and Pharmacology (London). 29(12):780-781, 1977.

To examine the relative functional availability of brain noradrenaline (NA) and dopamine storage pools, the NA metabolite, 3-methoxy-4-hydroxyphenylethylene glycol sulphate (MOPEG-SO4) was measured in rat brain following administration of centrally active alpha-adrenoreceptor blocking drugs with or without alpha-methyl-p-tryosine (alpha-MT) pretreatment. Both phenoxybenzamine and clozapine cause a marked increaese in MOPEG-SO4. Alpha-MT causes an insignificant lowering of the metabolite and a decrease in NA. Alpha-MT pretreatment did not significantly affect MOPEG-SO4 concentrations. Results suggest, that unlike the dopamine system, both newly synthesized and stored NA are readily available for neurogenic release at least under conditions of heavy demand. Taken in conjunction with previous studies, data suggest that in the NA system exchange between storage and functional sites occurs readily, or alternatively, the functional pool represents a very large proportion of the total NA content. 16 references.

001192 Meltzer, Herbert Y.; Fessler, Richard G.; Simonovic, Miljana; Doherty, John; Fang, Victor S. Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL **Lysergic acid diethylamide: evidence for stimulation of pituitary dopamine receptors.** Psychopharmacology (Berlin). 54(1):39-44, 1977.

The effects of lysergic acid diethylamide (LSD) on prolaction secretion in the rat were investigated to further determine it dopamine and 5-hydroxytryptamine (5-HT) agonist antagonist properties. LSD 0.05mg/kg and 0.20mg/kg significantly decreased plasma prolactin (PRL) levels in male rats. LSD 0.20 mg/kg, also inhibited the increase in plasma PRL levels produced by chlorpromazine and alpha-methylpara-tyrosine, both of which interfere with dopaminergic inhibition of PRL secretion. LSD was more potent than methysergide, a serotonin receptor blocker, in lowering plasma PRL levels and more potent than apomorphine, a known direct acting dopamine agonist, in blocking the increase in plasma PRL produced by quipazine, a 5-HT agonist. These results suggest LSD has potent dopamine agonist properties on the rat pituitary or hypothalamic dopamine receptors which directly or indirectly inhibit PRL secretion. 54 references. (Author abstract modified)

001193 Mendelow, A. David; Eidelman, B. H.; McCalden, T. A.; Rosendorff, C. University of the Witwatersrand Medical School, Johannesburg, South Africa **The effect of steroid hormones on cerebral blood flow before and after intracarotid infusion of 5-hydroxytryptamine.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):206-207, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, the effect of steroid hormones on the blood-brain barrier mechanism of sensitization of the cerebral vasculature to 5-hydroxytryptamine (5-HT) was studied in four groups of baboons. Estrogen, progesterone, monoamine oxidase inhibitor (tranylcypromine), and dexamethasone were administered before 5-HT, and regional cerebral blood flow and cerebral metabolism were measured before and after infusions. Pretreatment with monoamine oxidase inhibitor, estrogen, and progesterone changed cerebrovascular sensitivity to intracarotid 5-HT, significantly reducing cerebral blood flow, and dexamethasone did not. It was concluded that a steroid/monoamine oxidase/5-HT imbalance may be related to the vasospasm seen in the prodromal phase of migraine. 10 references.

001194 Meyer, Jerrold S.; Boggan, William O. Rockefeller University, 1230 York Ave., New York, NY 10021 **The effects of methaqualone on pituitary-adrenocortical activity in mice.** Psychopharmacology (Berlin). 54(1):51-55, 1977.

The acute and chronic effects of methaqualone on pituitary/adrenocortical activity in mice indicated by changes in plasma corticosterone content were examined. It was found that methaqualone produces a dose and time dependent increase in plasma corticosterone concentration in mice. Acute studies showed that this effect is largely independent of methaqualone induced hypothermia but can be blocked by pretreatment with dexamethasone, thus demonstrating that the adrenal cortex is not being directly stimulated. It was not clear whether the pituitary/adrenal activation is primarily caused by methaqualone itself or by a hepatic metabolite since pretreatment with SKF515-A failed either to potentiate or block the effect. Studies employing chronic methaqualone administration provided evidence for a rapid development of tolerance to the pituitary/adrenal effect of the drug. A parallel between plasma concentrations of methaqualone and the stimulation of pituitary/adrenal activity was found. Futhermore, drug concentrations 1 hour following methaqualone administration were diminished in chronically pretreated animals as compared to those previously untreated, suggesting that an altered metabolism of methaqualone may be responsible for the development of tolerance. 27 references. (Author abstract modified)

001195 Midha, K. K.; Bailey, K.; Hubbard, J. W.; Cooper, J. K. Drug Research Laboratory, Health Protection Branch, Health and Welfare, Ottawa, Canada **alpha-Methyldopamine -- a metabolite and key intermediate in the metabolic disposition of 3,4-methylenedioxyamphetamine** (MDA) **in dog and monkey.** Pharmacologist. 19(2):163, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the products formed by in vivo metabolism of 3,4-methylenedioxyamphetamine (MDA) in the dog and monkey was reported. The important metabolites separated from the urine of these species and identified were alpha-methyldopamine (MD), 3-0-methyl-alpha-methyldopamine, 3,4-dihydroxybenzyl methyl ketone, and, in the dog only, 4-hydroxybenzoic acid. It is suggested that MD may have a role in the overall pharmacologic activity of MDA, which includes the production of distinct visual and auditory sensory changes, sympathomimetic activity, interference with monoamine oxidase, and increased muscular rigidity in a patient with Parkinson's disease. (Author abstract modified)

001196 Miller, H. H.; Shore, P. A. University of Texas Health Science Center, Dallas, TX 75235 **Differing actions of amfonelic acid (AFA) and amphetamine (AMPH) on striatal dopamine (DA).** Pharmacologist. 19(2):239, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the actions of the nonamphetaminelike stimulant amfonelic acid (AFA) and of dextroamphetamine on newly formed dopamine (DA) in rat

striatal tissue was reported. AFA showed an effect on the metabolism of newly synthesized DA similar to that previously demonstrated on performed DA, i.e.,a decrease in striatal DA and an increase in striatal DA metabolites when tested in the presence of haloperidol and a hastening of the decline in DA produced by haloperidol plus DA synthesis blockade by alpha-methyltyrosine. Dextroamphetamine, in the presence of haloperidol, increased radiolabeled DA and decreased radiolabeled DA acidic metabolites. Monoamine oxidase inhibition was not a major factor since dextroamphetamine raised radiolabeled DA concentration even in haloperidol plus pargyline treated rats. Similar actions of dextroamphetamine were seen on total preformed DA. Dextroamphetamine raised total DA with or without haloperidol even in the presence of pargyline, and also slowed the rate of DA decline produced by haloperidol plus alpha-methyltyrosine. It is suggested that amphetamine may release DA from a special site, with some of the released DA entering the DA storage system. 1 reference. (Author abstract modified)

001197 Modak, Arvind T.; Stavinoha, William B. Department of Pharmacology, University of Texas Health Science Center, San Antonio, TX 78274 **The effect of nicotine on the acetylcholine content in mouse brain regions.** Pharmacologist. 19(2):221, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effect of nicotine on acetylcholine (ACh) levels in mouse brain regions was reported. The study was performed to identify nicotine receptor areas in vivo. Nicotine administered intravenously 10 min prior to sacrifice by mircowave irradiation significantly increased ACh levels in the corpus striatum, midbrain, and diencephalon but not in cerebellum, medulla/pons, hippocampus, or spinal cord. (Author abstract modified)

001198 Mohler, H.; Okada, T. Pharmaceutical Research Department, F. Hoffmann-La Roche, CH-4002 Basel, Switzerland **Benzodiazepine receptor: demonstration in the central nervous system.** Science. 198(4319):849-851, 1977.

The identification of a benzodiazepine receptor in the rat central nervous system (CNS), identified by high affinity (3H)diazepam binding, is reported. The receptor is mainly localized in the synaptic membrane fraction, and binding is stereospecific. Competition for the receptor by various benzodiazepines closely parallels their respective pharmacological potency. It is noted that the benzodiazepine receptor in human brain corresponds to that of rat brain in affinity stereospecificity and regional distribution. 11 references. (Journal abstract modified)

001199 Mosnaim, A. D.; Mason M.; Silkaitis, R. P.; Vazquez, A. J. Chicago Medical School, Chicago, IL 60612 **Phenylethylamines as mediators of the CNS effects of amphetamine.** Pharmacologist. 19(2):195, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the possible role of phenylethylamines as mediators of the CNS effects of amphetamine was reported. The increase in exploratory activity observed in mice after administration of racemic amphetamine was not suppressed by acute or chronic pretreatment with alpha-methyl-paratyrosine, which depletes norepinephrine (NE) and dopamine (DA). Pretreatment with alpha-methyldopa, which depletes NE, DA, and phenylethylamine (PEA), prevented the increase in exploratory activity. Amphetamine raised brain PEA levels after intraventricular administration of radiolabeled L-phenylalanine by increasing in situ CNS PEA biosynthesis. These results, along with the previous finding that administration of amphetamine after administration of intraventricular radiolabeled PEA decreases the recoveries of PEA and phenylacetic acid and increases PEA conversion to paratyramine, thus also possibly increasing DA formation, suggest that PEA itself or some of its metabolites are involved in the CNS effects of amphetamine. 1 reference. (Author abstract modified)

001200 Muller, P.; Seeman, P. Dept. of Pharmacology, University of Toronto, Toronto, Ontario M5S 1A8, Canada **Brain neurotransmitter receptors after long-term haloperidol: dopamine, acetylcholiner, serotonin, alpha-noradrenergic and naloxone receptors.** Life Sciences (Oxford). 21(12):1751-1758, 1977.

Because long-term neuroleptic therapy is known to alter brain dopaminergic sensitivity, the effects of chronic haloperidol administration (10mg/kg/day for 3 weeks) on the amount of the dopamine receptors were studied in various regions of rat brain. To test whether the changes in dopamine receptors were selectively produced, acetylcholine receptors, alpha-noradrenergic receptors, 3H-serotonin receptors, and 3H-naloxone receptors were assayed. The specific binding of 3H-haloperidol increased significantly by 34% in the striatum and by 45% in the mesolimbic region after long-term haloperidol. The specific binding of 3H-apomorphine also increased significantly by 77% in the striatum and 55% in the mesolimbic area. Although there was a small significant increase of 20% in specific 3H-serotonin binding in the striatum, no such increment occurred in the hippocampus or the cerebral cortex. No significantly different binding occurred for the other 3H-ligands in these brain regions except for a 13% increase in alpha-noradrenergic binding in the cerebral cortex. These results indicate that long-term haloperidol treatment produces rather selective increases in dopamine/neuroleptic receptors, without much change in four other types of receptors. Such relatively selective increments in these receptors may be the basis of dopaminergic supersensitivity (e.g. tardive dyskinesia) after long-term haloperidol. 57 references. (Author abstract modified)

001201 Mussini, E.; Marcucci, F.; Airoldi, L.; Facchinetti, T.; Garattini, S. Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea, 62, I-20157 Milano, Italy **Hydroxylation of three benzodiazepines in vitro.** Journal of Pharmaceutical Sciences. 66(10):1482-1483, 1977.

Three structurally related benzodiazepines were studied as substrates for hydroxylation by liver microsomal enzymes of rats and mice. The Vmax was comparable for dechlorodesmethyldiazepam, desmethyldiazepam, and 2'-chlorodesmethyldiazepam in the two animal species. The apparent Km decreased from dechlorodesmethyldiazepam to 2'-chlorodesmethyldiazepam for liver microsomal enzymes from both animal species. The hydroxylation of desmethyldiazepam and 2'-chlorodesmethyldiazepam yielded two pharmacologically active metabolites, oxazepam and lorazepam, respectively. 17 references. (Author abstract)

001202 Myslinski, Norbert R.; Thut, Paul D. Dept. of Pharmacology, School of Dentistry, University of Maryland, Baltimore, MD 21201 **The effect of 5,6-dihydroxytryptamine on post-decapitation convulsions.** Life Sciences (Oxford). 21(10):1475-1482, 1977.

To test the involvement of the serotonergic system in the prolongation of postdecapitation convulsions (PDC) in mice, L-DOPA (320mg/kg) was administered to mice 3 weeks after pretreatment with the 5-hydroxtryptamine (5-HTP) neurotoxin, 5,6-dihydroxytryptamine (5,6-DHT). All mice were given the peripheral decarboxylase inhibitor, Ro 4-4602. 5,6-DHT halved the brain 5-HT levels and significantly increased the duration of clonic PDC. The administration of L-DOPA to 5,6 DHT treated mice did not produce any further significant increases in duration. The administration of 5-hydroxytryptophan (5-HTP) to 5,6-DHT treated mice, however, increased 5-HT to above control levels and reduced convulsions to control levels. Administration of both 5-HTP and L-DOPA to 5,6-DHT treated mice resulted in 5-HT levels and convulsion times which were also not significantly different from the controls. These data indicate that intact 5-HT nerve terminals are necessary for L-DOPA to prolong the duration of clonic PDC. 25 references. (Author abstract modified)

001203 Natsuki, Reiko; Hitzemann, Robert J.; Hitzemann, Barbara A.; Loh, Horace H. Department of Pharmacology, University of California, San Francisco, CA 94143 **Effect of pentobarbital on regional brain phospholipid synthesis.** Biochemical Pharmacology (Oxford). 26(22):2095-2100, 1977.

To examine the effect of pentobarbital on regional brain phospholipid synthesis, male Sprague-Dawley rats were given 45mg/kg intraperitoneally sodium pentobarbital 15 min prior to the intraventricular injection of 200muCi (32P)phosphoric acid and 50muCi (3H)glycerol. The animals were sacrificed 1 hr later, subcellular fractions were prepared from four subcortical brain regions and phospholipids were extracted. Pentobarbital significantly increased the ratio of (3H) and (32P)triphosphatidylinositol (TPI) to diphosphatidylinositol (DPI) in the microsomal but not synaptosomal fractions. The possible relationship of this change to nicotinic receptor activity is discussed. Pentobarbital specifically decreased 32Pi but not (3H)glycerol incorporation into synaptosomal phosphatidylinositol (PI). Thus, pentobarbital induced the opposite of the neurotransmitter effect on PI turnover. Pentobarbital either decreased or had no effect on the incorporation of 32Pi and (3H)glycerol into phosphatidylserine (PS), phosphatidylcholine (PC) and phosphatidylethanolamine (PE). 34 references. (Author abstract modified)

001204 Nazar, Barry; Kairys, David J.; Fowler, Ronald; Harclerode, Jack. Department of Medicine, Milton S. Hershey Medical College, Hershey, PA **Effects of delta9-tetrahydrocannabinol on serum thyroxine concentrations in the rat.** Journal of Pharmacy and Pharmacology (London). 29(12):778-779, 1977.

To examine the effects of delta9-tetrahydrocannabinol (THC) on serum thyroxine concentrations, circulating thyroxine concentrations were assessed in rats on acute and chronic treatment schedules. Acute administration of THC depresses serum thyroxine concentrations: single injection depresses thyroxine after 6 hr; and administration of thyroid stimulating hormone (TSH) elicits an elevation of serum thyroxin suggesting a central effect and indicating that THC acts indirectly on thyroid function. Chronic THC treatment results in the development of a tolerance to thyroid depressant actions as well as to hypothermic actions of THC, and to depression of cellular respiration. A further study indicates that the presence of adrenal hormones is not required for depression of thyroid function by THC. 5 references.

001205 Nemtsov, A. V.; Rad'ko, K. A. Otdel psikhofarmakologii, Moskovskiy NII psikhiatrii, Ministerstva zdravookhreneniya RSFSR, Moscow, USSR /**Influence of chlorpromazine and trifluoperazine on neurons of an isolated slab of rabbit cerebral cortex.**/ Deystviye aminazina i triftazina na neyrony izolirovannoy poloski kory mozga krolikov. Zhurnal Vysshey Nervnoy Deyatel'nosti (Moskva). 27(3):651-653, 1977.

The hypothesis that in cases of neuronal isolation, cerebral neurons do not react to neuroleptics such as chlorpromazine and trifluoperazine was tested. In an experiment, slabs of rabbit cerebral cortex were isolated and treated with the drugs and changes were recorded with microelectrodes. Thirteen specific neurons were examined, revealing that after administration of the neuroleptics the average frequency of impulses dropped. The effects of the neuroleptics are in many ways similar to the effects of local anesthetics, which increase critical spike potentials. The precise mechanism by which the neuroleptics exert this effect remains to be determined. 9 references.

001206 Neuser, Volker; Hoffmeister, Friedrich. Institute of Pharmacology, Bayer AG, West Germany **The influence of psychotropic drugs on the local cerebral glucose-utilisation of the rat.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):102-103, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, the influence of psychotropic drugs d-amphetamine, diazepam, and heroin on the glucose utilization of a variety of cerebral regions of the rat was studied using a labeled tracer method. Sectioned brains of treated animals were quantitatively autoradiographed, densitometrically analyzed, and the glucose utilization calculated. Diazepam reduced glucose utilization in the thalamic, hypothalamic, and limbic structures, corresponding to an antianxiety effect. D-amphetamine increased glucose utilization of all brain structures investigated except the auditory pathway. Heroin diminished glucose utilization of cortical and subcortical brain areas, attributed to sedative effects in larger doses; smaller doses increased utilization in the dopaminergic system and in structures of the pain/temperature pathway. Results demonstrated that these psychotropic drugs modified local cerebral glucose utilization of the rat characteristically, corresponding with some drug dependent alterations of behavior. 3 references.

001207 Nielsen, Jann A.; Sparber, S. B. University of Minnesota, Minneapolis, MN 55455 **Effects of d-amphetamine (d-A), prostaglandin (PG) E1 and F-2alpha on 3H-2-dopamine (3H-DA) metabolism, fixed interval (FI) behavior and rectal temperature.** Pharmacologist. 19(2):149, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of various doses of prostaglandin E-1 (PGE1) or prostaglandin F-2alpha (PGF2alpha) plus radiolabeled dopamine (DA) administered via lateral ventricular cannulas and of the effects of intraperitonial dextroamphetamine on DA metabolism, fixed interval (FI) behavior, and rectal temperature in rats was reported. PGF2alpha significantly decreased, while PGE1 significantly increased, the concentrations of the DA metabolites, 3, 4-dihydroxyphenylacetic acid, homovanillic acid, and 3-methoxytyramine. Both PGs decreased 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG). PGF2alpha did not affect FI behavior; PGE1 caused seizures during testing. Hyperthermia was produced by PGE1 and by the highest dose of PGF2alpha. Dextroamphetamine significantly decreased DA metabolism but increased the concentration of MHPG. Behavior was al-

tered in a rate dependent manner; temperature was unaffected. Dextroamphetamine produced hypothermia when administered in conjunction with PGF2alpha and blocked the hyperthermia caused by both PGs. It is concluded that PGE1 and PGF2alpha have opposite effects upon central DA metabolism and may modulate the actions of psychoactive drugs which alter CNS catecholamine concentrations. (Author abstract modified)

001208 Nixon, Ralph A.; Karnovsky, Manfred L. Department of Neurology, University of Vermont College of Medicine, Burlington, VT 05401 **Uptake and metabolism of intraventricularly administered piperidine and its effects on sleep and wakefulness in the rat.** Brain Research (Amsterdam). 134(3):501-511, 1977.

To examine uptake and metabolism of intraventricularly administered piperidine and its effects on sleep and wakefulness, piperidine, a pharmacologically active amine found in mammalian brain, was infused into the cerebral ventricles of freely moving rats. Doses of 1.0micrograms or greater induced EEG activation and complete suppression of desynchronized sleep in the initial 20 min period following the start of the infusion. In the next 2 h interval, when considerable amounts of exogenous piperidine were still measurable in the brain, the proportion of waking and slow wave sleep was comparable to that in baseline control records although the proportion of desynchronized sleep remained lowered. Dimethylamine, an aliphatic amine with only weak pharmacological activity, had little effect on EEG or EMG when infused intraventricularly at a dose of 10 micrograms. Efflux of infused (3H)piperidine from the brain in the first 4 h was exponential with a half-life of 30 min. The distribution of administered piperidine in the brain after giving high and low doses was similar to that of the uptake of dimethylamine. Highest concentrations were found in the hypothalamus, thalamus and mesencephalon, and lowest concentrations in the cerebral cortex. Differences in the rate of efflux of radioactivity from various brain regions were minor. The rate of piperidine catabolism was exceedingly slow; at 2 h after the infusion, (3H)piperidine still represented 98% of the tritium (excluding 3H2O) in the urine and 81% of that in the brain. The absence of storage, saturable high affinity uptake and rapid metabolism suggests that there is no mechanism for the rapid inactivation of piperidine in the brain, an important feature of putative neurotransmitters. In addition, the EEG results do not confirm a previously reported potent behavioral sedative effect of intraventricularly administered piperidine. 29 references. (Author abstract modified)

001209 Nordberg, A. Dept. of Pharmacology, Faculty of Pharmacy, University of Uppsala, Sweden **Modulation of acetylcholine turnover in brain regions and high affinity uptake.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):14, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the modulation of acetylcholine (ACh) turnover in brain regions and high affinity uptake into synaptosomes by pentobarbital (PB) and oxotrenorine (OXO), were studied in mice. PB and OXO increased the steady state concentrations of ACh in the hippocampus and cortex, and OXO increased ACh in the striatum. PB decreased apparent turnover only in the cortex and hippocampus; OXO was somewhat less specific. In agreement with the effect of PB and OXO on ACh turnover a decreased high affinity uptake of Ch was seen in synaptosomes from hippocampus and cortex. OXO also decreased the high affinity uptake in the striatum. 4 references.

001210 Novin-Baheran, A.; Mulvey, R. K. Wayne State University, Detroit, MI 48202 **Electroshock anticonvulsant activity and brain acetylcholine alterations in mice treated with select benzodiazepines.** Pharmacologist. 19(2):214, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the relationship between the antimaximal electroshock activity of benzodiazepines and their ability to alter brain acetylcholine (ACh) levels in mice was reported. The ED-50 for intraperitoneally injected clonazepam, diazepam, flurazepam, and nitrazepam against maximal electroshock induced convulsions were determined and the alterations of whole brain ACh levels 50 min to 60 min after administration of these doses of each drug were measured. Brain ACh levels were elevated 37% by diazepam, 9% by clonazepam, 8% by nitrazepam, and 6% by flurazepam. It is concluded that the ED-50 doses of these drugs which provide antimaximal electroshock activity promote increased brain ACh levels. (Author abstract modified)

001211 Olpe, H.-R.; Koella, W. P.; Wolf, P.; Haas, H. L. CIBA-Geigy Ltd., CH-4002 Basel, Switzerland **The action of baclofen on neurons of the substantia nigra and of the ventral tegmental area.** Brain Research (Amsterdam). 134(3):577-580, 1977.

The effects of iontophoretically or intraperitoneally applied beta-4-chlorophenyl-gamma-aminobutyric acid (baclofen) on neurons of the substantia nigra (NS) and of the ventral tegmental area (VTA) in the rat were compared to confirm and extend earlier studies showing a marked effect of baclofen on central neurons. Results indicate that baclofen does not interfere with stimulation induced inhibitions in the SN and VTA. Intraperitoneal and iontophoretic applications of baclofen resulted in depression of spontaneous firing in both SN and VTA; depressent effect of iontophoretic application were not antagonized by bicuculline applied in sufficient amounts to block gamma-aminobutyric acid (GABA) effects. Results suggest baclofen in schizophrenic patients may act by reducing dopaminergic influence upon postsynaptic cells in the striatum and accumbens. 20 references.

001212 Olsson, S.-O.; Passwal, M.; Refsum, H. AB Ferrosan, Malmo, Sweden **In vitro autonomic effects of four neuroleptics: chlorpromazine, haloperidol, melperone and thioridazine.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):66, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the in vitro autonomic effects of four neuroleptics were studied to elucidate anticholinergic (AC), antihistaminergic (AH), antiserotoninergic (AS), antialpha-adrenergic (AAA) and antibeta-adrenergic (ABA). Melperone differed from chlorpromazine, haloperidol, and thioridazine in possessing very slight AC and AH effects. Haloperidol had the same AAA effects as melperone, but was 50 times weaker than chlorpromazine and thioridazine. Melperone was a competitive AAA, but thioridazine was a noncompetitive AAA. All four neuroleptics had a slight AS effect. No significant ABA effect was demonstrated. It was suggested that in common therapeutic plasma concentrations, only the AAA effect of melperone may be manifest and none of the effects of haloperidol. With chlorpromazine and thioridazine both the AAA, AH, and AC effects may be effective.

001213 Ostrovskaia, R. U.; Voronina, T. A. Institut farmakologii AMN SSSR, Moscow, USSR /**Negative effects of**

bicuculline and thiosemicarbazide on the tranquillizing action of diazepam./ Antagonisticheskoe vliianie bikukullina i tiosemikarbazida na trankviliziruiushchie effekty diazepama. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 83(3):293-295, 1977.

Based on previous studies of the inhibitive effects of benzodiazepines, the role of GABAergic mechanisms in the tranquillizing action of diazepam was examined in rats. It was found that bicuculline, an GABAergic receptor specific blocking agent, and thiosemicarbazide, a brain GABA synthesis inhibiting agent, are capable of antagonizing diazepam effects and of reducing its tranquillizing activity in an experimental test of conflict behavior. Bicuculline shows more pronounced antagonism to diazepam than thiosemicarbazide. The data suggest possible involvement of the GABAergic mechanisms in the anxiolytic action of benzodiazepines. 11 references. (Journal abstract modified)

001214 Ott, T.; Bures, J. Institute of Pharmacology and Toxicology, Magdeburg, Germany **Monosynaptic activation of fascia dentata in unrestrained rats: response modification by synaptically active drugs.** Activitas Nervosa Superior (Praha). 19(2):158-160, 1977.

A paper delivered at the Second International CIANS Congress and concerned with testing the possible involvement of noradrenaline (NA) or acetylcholine (ACh) in the neurotransmission at the perforanth pathway (pp) area dentata synapse is presented. This involvement was tested by recording fascia dentata responses to pp stimulation in unrestrained rats under the influence of different synaptically active drugs (scopolamine, orecoline, ergotamine, and amphetamine). It is concluded that neither ACh nor NA is the neurotransmitter at the synapse under investigation. 9 references.

001215 Otten, U.; Schwab, M.; Gagnon, C.; Thoenen, H. Department of Pharmacology, Biocenter of the University, Basel, Switzerland **Selective induction of tyrosine hydroxylase and dopamine beta-hydroxylase by nerve growth factor: comparison between adrenal medulla and sympathetic ganglia of adult and newborn rats.** Brain Research (Amsterdam). 133(2):291-303, 1977.

The effect of nerve growth factor (NGF) in sympathetic ganglia and adrenal medulla of adult and newborn rats was investigated. Administration of NGF elicited a selective increase in tyrosine hydroxylase and dopamine beta-hydroxylase (DBH) both in sympathetic ganglia and adrenal medulla. This effect does not depend on intact preganglionic cholinergic fibers. The augmented enzyme activity results from enhanced enzyme synthesis since it can be abolished by cycloheximide and NGF has been shown to enhance the incorporation of (3H)leucine into DBH molecules. The responsiveness of the adrenal medulla to NGF is also supported by light and electron microscopic autoradiograms which show that intravenously injected (125I)NGF is accumulated with high selectivity in adrenal chromaffin as compared to adjacent adrenal cortical cells. In the adrenal medulla the difference between the effect of a single and 10 injections of NGF on enzyme induction was relatively small. In contrast, the effect on sympathetic ganglia was cumulative. 33 references. (Author abstract modified)

001216 Palmer, Gene C.; Wagner, H. Ryan; Palmer, Shelby J.; Manian, Albert A. Dept. of Pharmacology, University of South Alabama, College of Medicine, Mobile, AL 36688 **Histamine-stimulated adenylate cyclase: blockade by imipramine and its analogues.** Communications in Psychopharmacology. 1(1):61-69, 1977.

The role of histamine as a central neurotransmitter was studied through evaluation of a series of derivatives of the tricyclic antidepressant imipramine on the activation of adenylate cyclase by histamine using the rabbit cerebral cortex as a model system. Histamine sensitive adenylate cyclase was potently inhibited by imipramine and its chlorinated, desmethylated, and hydroxylated derivatives. This was evident when either incubated tissue slices or homogenates of rabbit cerebral cortex were used as an enzyme system. Furthermore, these agents did not influence the basal activity of the enzyme. The data are consistent with the postulated role of histamine as a central neural transmitter with possible involvement in affective disorders. 19 references. (Author abstract modified)

001217 Parfitt, Andrew; Klein, David C. Laboratory of Biomedical Sciences, National Institute of Child Health and Human Development, Bethesda, MD 20014 **Increase caused by desmethylimipramine in the production of (3H)melatonin by isolated pineal glands.** Biochemical Pharmacology (Oxford). 26(9):904-905, 1977.

The increase caused by desmethylimipramine (DMI) in the production of labeled melatonin by isolated pineal glands was investigated in a culture medium of pineal glands from Sprague-Dawley rats incubated with labeled tryptophan and treated with DMI. Animals were housed prior to decapitation in a room with an automatically regulated lighting schedule. A dose dependent increase in both N-acetyltransferase activity and labeled melatonin production was observed in animals where pineal glands were treated with DMI. Lower concentrations of DMI were also studied to gauge alteration of pineal indole metabolism, demonstrating an apparent sensitizing effect of DMI for drug effects (inhibition or uptake). Results suggest that if melatonin production in humans is regulated through an adrenergic mechanism similar to that in the rat, DMI treatment might increase melatonin production in humans, with some observed effects of DMI treatment being mediated by the pineal gland. 13 references.

001218 Pochatov, Yu. M.; Raevskiy, K. S. Laboratoriya neyrokhimicheskoy farmakologii, Institut farmakologii AMN SSSR, Moscow, USSR **/Action of azabutyrone and its analogs on catecholamine metabolism in rat brain./** Vliyanie azabutirona i ego analogov na obmen katekholaminov v mozge krys. Farmakologiya i Toksikologiya (Moskva). 40(1):5-8, 1977.

Action of the neuroleptic azabutyrone and its analogs on the accumulation and disappearance of 3H-norepinephrine and 3H-dopamine was studied in rats, using 3H-tyrosine, a tagged catecholamine precursor. Azabutyrone was shown to be able to accelerate dopamine circulation rate and norepinephrine circulation rate in rat brain. The diazabicyclodekanyl derivative produced a more marked effect than azabutyrone on amine circulation. Further weighting of the diazabicyclic radical and substitution of chlorine for fluorine in para position of the butyrophenone ring led to weakening of this effect. 12 references. (Journal abstract modified)

001219 Ransom, Bruce R.; Greenwood, Robert S.; Goldring, Sidney; Letcher, Frank S. Department of Neurology, Stanford University School of Medicine, Palo Alto, CA **The effect of barbiturate and procaine on glial and neuronal contributions to evoke cortical steady potential shifts.** Brain Research (Amsterdam). 134(3):479-499, 1977.

To elucidate the effects of barbiturate and procaine on glial and neuronal contributions to evoked cortical steady potential (SP) shifts, the direct cortical response in cats was studied simultaneously with intracellular recording from glia in one

group of experiments and with measurements of (K+)0 in another. Barbiturate produced the expected increase in the negative SP shift, but had either no effect, or slightly reduced glial slow depolarization (SD). The effect on (K+)0 was similar. These findings argue against glial SD as being the only source of the SP shift during barbiturate anesthesia and suggest a significant neuronal contribution. That this is so is strongly suggested by finding a reversal polarity of the barbiturate augmented negative SP shift, 600 to 900 micrograms below the cortical surface. With procaine, the SP shift and SD are modified similarly. They both undergo a quantitatively appropriate amplitude reduction. Laminar analysis of the reduced negative SP shift after procaine is qualitatively similar to the finding before giving the drug; there is no reversal. The reduced SP shift after procaine may continue to reflect glial SD. Procaine can diminish both direct and synaptic neural excitation which would result in a smaller extracellular liberation of K+ and hence a smaller glial SD and SP shift. By contrast, barbiturate which can also depress synaptic excitation is believed, in addition, to uncover and enhance (especially by prolongation) postsynaptic inhibition. Thus, after barbiturate, the augmented SP shift may reflect the addition of two separately generated surface negatives -- glial SD and summated hyperpolarizing inhibitory postsynaptic potentials in cortical depth. 47 references. (Author abstract modified)

001220 Rastogi, R. B.; Singhal, R. L.; Lapierre, Y. D. Department of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada **Involvement of central noradrenergic system in the mediation of behavioral suppressant effects of diazepam in hyperthyroid rats.** Psychiatric Journal of the University of Ottawa (Ottawa). 2(3):97-101, 1977.

In a paper presented at a meeting of the Group-Without-a-Name International Psychiatric Research Society, Cincinnati, April 1977, the involvement of central noradrenergic system in the mediation of behavioral suppressant effects of diazepam in hyperthyroid rats was examined. Experiments compared the effect of diazepam on norepinephrine (NE) metabolism in the brains of normal and neonatally hyperthyroid rats. Chronic treatment with diazepam in normal rats for 15 days, beginning from the 16th day of age, decreased spontaneous locomotor activity to 49% of controls. Furthermore, this tranquilizer decreased the neuronal release of norepinephrine as evidenced by increased endogenous levels of this amine in all brain areas examined and lowered levels of 4-hydroxy-3-methoxyphenylglycol. Daily exposure of hyperthyroid rats to diazepam for 15 days antagonized L-triiodothyronine induced increases in behavioral activity as well as brain norepinephrine utilization. In contrast to normal rats, diazepam treatment in hyperthyroid animals decreased L-triiodothyronine stimulated rise in the rate of catecholamine synthesis to values which were not significantly different from those seen for normal controls. In view of the known functional involvement of noradrenergic neurons in arousal, aggressiveness and sham rage behavior, it is hypothesized that diazepam produces its tranquilizing effect in hyperthyroid animals by blocking the turnover of brain norepinephrine. 28 references. (Author abstract modified)

001221 Rehavi, Moshe; Maayani, Saul; Goldstein, Leon; Assael, Marcel; Sokolovsky, Mordechai. George S. Wise Center for Life Sciences, Tel Aviv University, Tel Aviv, Israel **Antimuscarinic properties of antidepressants: dibenzepin (Noveril).** Psychopharmacology (Berlin). 54(1):35-38, 1977.

The antimuscarinic potency of dibenzepin (Noveril) was estimated by measuring central in vivo effects in mice (antihypothermia and antitremor, both induced by oxotremorine), peripheral in vivo activity (mydriasis caused by systemic administration of the drug), the effects of dibenzepin on isolated smooth muscle from guinea-pig ileum, and in vitro determination of the affinity constant of dibenzepin toward the muscarinic binding sites in whole mouse brain homogenate. The data allowed the construction of a normalized antimuscarinic potency scale for some of the common tricyclic antidepressants. With a value of 1 for scopolamine, the following relative anticholinergic potencies were calculated: dibenzepin 1/600, nortriptyline 1/300, imipramine 1/200, and amitriptyline 1/75. These values suggest an explanation for the absence of clinically detectable anticholinergic side-effects during treatment of depression with high doses of dibenzepin. Structural and spatial interrelations among various tricyclic antidepressants and scopolamine are discussed. 12 references. (Author abstract modified)

001222 Richards, J. G. Pharmaceutical Research Department, F. Hoffmann-La Roche, CH-4002 Basel, Switzerland **Autoradiographic evidence for the selective accumulation of (3H)5-HT by supra-ependymal nerve terminals.** Brain Research (Amsterdam). 134(1):151-157, 1977.

Several periventricular regions of rat brain were investigated for their ability to accumulate (3H)5-HT. The possible effects of known antidepressants (5-HT or noradrenaline uptake inhibitors) on the accumulation of (3H)5-HT in a pure serotoninergic nerve terminal network were also investigated. Results indicate that the physiological significance of the specific uptake mechanism in supraependymal nerve terminals is likely to be removal of 5-HT from synaptic areas to terminate the possible neurotransmitter action of 5-HT. At present the effector organ (target cell) is not known, although several hypothesis are put forward. It is concluded that supraependymal nerve terminals possess a specific uptake mechanism for 5-HT which is inhibited by chlorimipramine but not by desmethylimipramine. Clinically, potent 5-HT uptake inhibitors have predominantly mood elevating properties and/or sedative, antianxiety effects. 24 references.

001223 Richelson, Elliott; Divinetz-Romero, Silvia. Mayo Foundation, Dept. of Psychiatry, Rochester, MN **Blockade by psychotropic drugs of the muscarinic acetylcholine receptor in cultured nerve cells.** Biological Psychiatry. 12(6):771-785, 1977.

The ability of antimuscarinics, tricyclic antidepressants, and antipsychotics to block the muscarinic acetylcholine receptor was determined using an assay for this receptor in cultured nerve cells. The technique involved the assay of receptor mediated formation of guanosine-3,5-cyclic phosphate (cyclic-GMP) from radioactively labeled guanosine-5-triphosphate in living mouse neuroblastoma cells (clone N1E-115). This cyclic-GMP formation occurred rapidly (peak at 30 sec) and was dependent on the concentration of agonist. The psychotropic drugs tested blocked the muscarinic receptor and equilibrium dissociation constants were calculated from the parallel displacement of dose response curves. The most potent compound was the antimuscarinic dexetimide, while the least potent was the antipsychotic prochlorperazine. All tricyclic antidepressants with tertiary amine side-chains were more potent than those with secondary amine side-chains; whereas phenothiazine potency correlated with the side-chain structure as follows: piperadine greater than alkylamine greater than or equal to piperazine. These data for psychotherapeutic drugs may have direct clinical application. 29 references. (Author abstract)

001224 Riffee, William H.; Ludden, Thomas D.; Gerald, Michael C. College of Pharmacy, University of Texas, Austin, TX 78712 **Comparative brain/plasma concentrations of amphetamine isomers in mice.** Pharmacologist. 19(2):195, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study comparing the brain and plasma concentrations of dextroamphetamine and levoamphetamine as a function of dose and time after administration of the radiolabeled isomers to mice was reported. Thirty min after 2.5mg/kg, 5mg/kg, 10mg/kg, and 15mg/kg intraperitoneally (ip), brain dextroamphetamine/levoamphet amine concentration ratios were 1.96, 2.08, 1.31, and 0.83, respectively. Plasma ratios followed a similar pattern but were somehwat higher. The ratio of dextroamphetamine/levoamphet amine was consistently higher in brain and plasma 7.5min to 120 min after 2.5mg/kg and 10mg/kg. By contrast, after intravenous (iv) administration of these doses, no isomeric differences in brain amphetamine were noted at 7.5min to 120 min, although plasma dextroamphetamine/levoamphetamine ratios were increased. After SKF 525A pretreatment, the dextroamphetamine/levoamphetamine ratios after ip administration were similar to those seen after iv injections. It is suggested that after ip administration, levoamphetamine has a higher volume of distribution than does dextroamphetamine, and may also be metabolized more rapidly, resulting in lower plasma concentrations and thus reducing the levels that reach the brain. (Author abstract modified)

001225 Robinson, S. E.; Cheney, D. L.; Moroni, F.; Costa, E. Saint Elizabeth's Hospital, National Institute of Mental Health, Washington, DC 20032 **Effect of nomifensine and other antidepressant drugs on acetylcholine turnover in various areas of rat brain.** Pharmacologist. 19(2):221, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study comparing the effects of nomifensine (N) and other antidepressant drugs on acetylcholine turnover (TR-ACh) in various areas of rat brain was reported. N increased TR-ACh in the cortex, hippocampus, and diencephalon, whereas desipramine and chlorimipramine decreased TR-ACh in the striatum and hippocampus. Amitriptyline had no significant effect in the areas studied. Iprindole increased TR-ACh in the hippocampus. N had the same pattern of action as amphetamine on cortical and hippocampal TR-ACh but failed to mimic apomorphine. Intraseptal phenoxybenzamine blocked the N induced and amphteamine induced increases in TR-ACh in the cortex and hippocampus, suggesting that N operates via noradrenergic septal synapses. (Author abstract modified)

001226 Robinson, Susan E.; Lotti, Victor J.; Sulser, Fridolin. Tennessee Neuropsychiatric Institute, Vanderbilt University School of Medicine, 1501 Murfreesboro Road, Nashville, TN 37217 **Cyanocyproheptadine: role of cholinolytic properties in modulating neuroleptic-induced elevation of striatal homovanillic acid (HVA).** Journal of Pharmancy and Pharmacology (London). 29(9):564-566, 1977.

The cholinolytic and neuroleptic properties of dextro-3-cyanocyproheptadine, levo-3-cyanocyprophetadine, and racemic 3-cyanocyproheptadine were examined to determine their roles in modifying the neuroleptic induced elevation of striatal homovanillic acid (HVA) in animals. The levorotatory isomer was 3 times more potent a neuroleptic than chlorpromazine in squirrel monkeys and had weak or no cholinolytic properties in mice. The dextrorotatory isomer showed 3 to 6 times more cholinolytic activity than clozapine but exhibited no neuroleptic activity. The racemic compound was more potent as an oxotremorine antagonist than was the dextrorotatory isomer; it is suggested that this is probably the result of this isomer's combined neuroleptic and cholinolytic properties. Levo-3-cyanocypropheptadine produced a significant dose dependent increase in the concentration of HVA in rat striatum, while dextro-3-cyanocypropheptadine had no effect on striatal HVA. The racemic compound produced alterations in HVA concentration which were not significantly different from those achieved with the levorotatory isomer alone, suggesting that factors other than cholinolytic activity may be responsible for the observed reduction in HVA when certain cholinolytic compounds are administered in combination with a neuroleptic drug. The pharmacology of the racemic mixture of 3-cyanocyproheptadein suggests that strong cholinolytic properties of a drug do not necessarily preclude a neuroleptic profile. 16 references.

001227 Roffman, Mark; Cassens, Geraldine; Schildkraut, Joseph J. Department of Pharmacology, CIBA-Geigy Corporation, Summit, NJ 07901 **The effects of acute and chronic administration of morphine norepinephrine turnover in rat brain regions.** Biochemical Pharmacology (Oxford). 26(24):2355-2358, 1977.

The effects of acute and chronic administration of morphine on norepinephrine turnover in rat brain regions were assessed by measuring changes in the levels of 3-methoxy-4-hydroxyphenylglycol sulfate (MHPG-SO4), the major metabolite of norepinephrine (NE) in rat brain. Acute administration of morphine sulfate (25mg/kg) significantly increased levels of MHPG-SO4 in hypothalamus, cerebellum, brainstem and rest of brain not in cortex or corpus striatum. After chronic administration of increasing doses of morphine, tolerance developed to this effect of morphine on MHPG-S04 levels in cerebellum, brainstem and rest of brain, but in MHPG-SO4 levels was not observed in hypothalamus. Sixteen hr after the cessation of chronic morphine administration, levels of MHPG-SO4 were significantly reduced in hypothalamus, cerebellum and rest of brain. These findings are discussed in relation to the regional specificity of the action of morphine on NE turnover, and the possible role of noradrenergic neurons in the reinforcing properties of morphine. 17 references. (Author abstract)

001228 Roffman, Mark; Kling, Mitchel A.; Cassens, Geraldine; Orsulak, Paul J.; Reigle, Thomas G.; Schildkraut, Joseph J. CIBA-GEIGY Inc., Department of Pharmacology, Summit, NJ 07901 **The effects of acute and chronic administration of tricyclic antidepressants on MHPG-S04 in rat brain.** Communications in Psychopharmacology. 1(3):195-206, 1977.

The effects of acute and chronic administration of various tricyclic antidepressants on the levels of 3-methoxy-4-hydroxyphenylglycol sulfate (MHPG-SO4), the principal metabolite of norepinephrine (NE) in rat brain, were examined. The levels of MHPG-SO4 were significantly decreased after acute administration of desmethylimipramine or imipramine and tended to be decreased after nortriptyline but not after amitriptyline. However, after chronic administration for 2 weeks, the levels of MHPG-SO4 were significantly increased by desmethylimipramine or imipramine and were slightly increased by nortriptyline or amitriptyline. These results may help to explain why sustained treatment with tricyclic antidepressants is required to achieve clinical antidepressant effects. 29 references. (Journal abstract)

001229 Roizen, M. F.; White, P. F.; Eger, E. I., II; Brownstein, Michael J. Depts. of Anesthesia and Medicine, Univ. of California, San Francisco, CA **The effect of ablation of serotonin or norepinephrine brain stem areas on halothane and cyclopropane MAC in rats. (Unpublished paper).** Bethesda, MD, NIMH, 1977. 10 p.

The anesthetic requirements of rats having destructive lesions in either the locus coeruleus, ventral noradrenergic bundle, or the nucleus raphe dorsalis were compared with that of control animals to test the hypothesis that anesthesia results from interruption of nervous transmission in specific discrete brain areas rather than from a generalized depression of transmission. Findings show that destruction of the ventral bundle, which supplies approximately 40% of the norepinephrine in the central gray catecholamine area, decreased halothane MAC 35% and cyclopropane MAC 16%. Ventral bundle lesions decreased hypothalamic norepinephrine by 90% without altering cortical or cerebellar norepinephrine. Lesions in the serotonin rich nucleus raphe dorsalis decreased halothane MAC 25% and cyclopropane MAC 16. These lesions decreased hypothalamic serotonin content by 40%, and cortical and cerebellar serotonin content by 80%. It is concluded that although destruction of individual nuclei significantly decreased anesthetic requirement, no specific nucleus appears to be of primary importance. 22 references. (Author abstract modified)

001230 Ronai, Andras Z.; Berzetei, Ilona; Bajusz, Sandor. Research Institute for Pharmaceutical Chemistry, H-1325 Budapest, PO Box 82, Hungary **Differentiation between opioid peptides by naltrexone.** European Journal of Pharmacology (Amsterdam). 45(4):393-394, 1977.

An attempt to differentiate between synthetic pentapeptides by antagonizing them with naltrexone in both guinea-pig ileum and mouse vas deferens was made. It was found that in guinea-pig ileum, the action of all peptides can be counteracted by naltrexone to the same extent as that of nonpeptide narcotics. In mouse vas deferens most of the peptide derivatives can be antagonized with naltrexone by approximately one order of magnitude less than by normorphine. It is suggested that the interaction of the same receptor with discrete peptide, or still unknown nonpeptide ligands would induce a change in the receptor molecule, altering the kinetic characteristics of agonist/antagonist interaction. 4 references.

001231 Ross, David H. Department of Pharmacology, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284 **Calcium content and binding in synaptosomal subfractions during chronic morphine treatment.** Neurochemical Research. 2(5):581-593, 1977.

Chronic exposure to morphine in mice produced an increase in Ca2+ content of synaptosomes, synaptic plasma membranes (SPM), and synaptic vesicles. Ca2+ binding capacity was significantly reduced in tolerant SPM fractions. Naloxone significantly reversed the increased calcium content and reduced binding capacity of SPM when administered to 72 h treated mice. Scatchard analysis of binding curves reveals three distinct classes of Ca2+ binding sites. During tolerance, the high and low affinity sites exhibit a reduced capacity to bind calcium, which may be reversed by in vivo and in vitro administration of naloxone. The increase in SPM and synaptic vesicle calcium content may reflect adaptive changes in the cell membrane during tolerance development, which may contribute to changes in neurotransmitter and second messenger function. 30 references. (Author abstract)

001232 Ross, Svante B. Research and Development Laboratories, Astra Lakemedel AB, S-15185 Sodertalje, Sweden **On the mode of action of central stimulatory agents.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(4):392-396, 1977.

The mode of action of central stimulatory agents is examined in a letter to the editor. To investigate the hypothesis that amphetamine like agents act by release of extravesicular dopamine (DA) while the methylphenidate like agents act by inhibition of membrane DA uptake, the inhibitory potencies of (+)-amphetamine, (-)-amphetamine,(-)-ephedrine, phenmetrazine, methylphenidate, cocaine, Astra-2959b, and prolintane on the accumulation of labeled DA in cell free homogenates of striatum from normal and reserpinized rats were assessed. Data indicate that all the amphetamine like agents were potentiated by reserpine, while the inhibition by all methylphenidate like agents was uninfluenced by reserpine, thus providing support for the hypothesis. Possible association between membranal dopamine regulation and schizophrenia is briefly discussed. 12 references.

001233 Ross, Svante B.; Ogren, Sven-Ove; Renyi, Anna L. Research and Development Laboratories, Astra Lakemedel AB, S-15185 Sodertalje, Sweden **Substituted amphetamine derivatives. I. Effect on uptake and release of biogenic monoamines and on monoamine oxidase in the mouse brain.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(4):337-352, 1977.

The effects of amphetamine (A), 2-, 3- and 4-chloramphetamine (CA), 4-methylamphetamine (MA) and chlorphentermine (CP) in inhibiting the accumulation and in evoking release of of radioactive labelled noradrenaline (NA), dopamine (DA) and 5-hydroxytryptamine (5-HT) and in inhibiting the oxidative deamination of tyramine and 5-HT in mouse brain slices (midbrain and striatum) were examined. The inhibitory potencies on the NA uptake in vitro and after intraperitoneal administration varied only slightly, 3-CA being the most potent and 2-CA the least active compound. The structure activity for inhibition of the DA uptake in striatal slices was similar with the exception that CP was the least potent agent. The accumulation of 5-HT was most potently inhibited by the 4 and 3-substituted amphetamines. Only a small (20%) fraction of the (3H)NA accumulated in the midbrain slices could be released by the amphetamines but a significant release was obtained at rather low concentrations. The release of radioactive DA and 5-HT from striatal slices was much more pronounced and the orders of activities were similar to those for the inhibition of the accumulation of DA and 5-HT, except that CP was comparatively less active in releasing 5-HT. The oxidative deamination of tyramine and 5-HT was most potently inhibited by 4-CA and 4-MA and this effect was obtained at the same doses producing inhibition of the amine uptake. No effect was obtained on the deamination of phenethylamine. 35 references. (Author abstract)

001234 Ruffolo, Robert R.; Patil, Popat N. College of Pharmacy, Ohio State University, Columbus, OH 43210 **Onset and offset of chlorpromazine blockade of phenylephrine, carbamylcholine and histamine on rabbit stomach strips.** Pharmacologist. 19(2):130, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the kinetics of receptor blockade by chlorpromazine on fundic strips from the rabbit stomach was reported. Blockade by chlorpromazine proceeded at identical rates when carbamylcholine and histamine were the agonists and occurred more slowly against

phenylephrine. Offset of blockade by chlorpromazine was also faster against carbamylcholine and histamine than against phenylephrine. No correlations were found between the kinetics of blockade and the potency of chlorpromazine or the various agonists for the receptors. It is suggested that alpha-adrenoreceptors in the rabbit stomach are less accessible to chlorpromazine than either the muscarinic or histaminic (H-1) receptors. (Author abstract modified)

001235 Samanin, R.; Bendotti, C.; Miranda, F.; Garattini, S. Instituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, I-20157 Milan, Italy **Decrease of food intake by quipazine in the rat: relation to serotoninergic receptor stimulation.** Journal of Pharmacy and Pharmacology (London). 29(1):53-54, 1977.

The effect of quipazine, a new type antidepressant drug, on food intake was studied in female Charles River rats weighing 200 to 250g. The rats were given 3mg/kg methergoline i.p. or the vehicle, followed 3 hr later by 2.5, 5, or 10mg/kg quipazine or saline i.p. Animals were then placed in a cage for 2 hr, and the amount of food intake was measured. In some animals, electrolytic lesions were made in the median raphe nucleus, and after recovery these rats were given 10mg/kg quipazine i.p. and food intake was measured. Serotonin levels were fluorimetrically determined in the forebrain 24 hr after the end of the experiment. Results showed quipazine produced a dose dependent reduction of food intake in the rats. This effect was antagonized by pretreatment with methergoline. This effect of quipazine was not significantly affected by the lesion in the median raphe nucleus. The forebrain concentration of serotonin was 0.32mcg/g in the sham operated rats and 0.11mcg/g in the lesioned rats. Since methergoline shows central antiserotonin activity and inhibits the effect of quipazine on food intake, quipazine probably acts by directly stimulating central serotonin receptors. 24 references.

001236 Samanin, R.; Jori, A.; Bernasconi, S.; Morpugo, E.; Garattini, S. Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, I-20157, Milan, Italy **Biochemical and pharmacological studies on amineptine (S 1694) and (+)-amphetamine in the rat.** Journal of Pharmacy and Pharmacology (London). 29(9):555-558, 1977.

The pharmacological and neurobiochemical activities of amineptine (S-1694) were compared with those of dextroamphetamine in rats. The locomotor activity, stereotyped behavior, and hypothermia induced by amineptine were similar to but not as marked as those produced by dextroamphetamine, and there was little or no anorectic action. Amineptine did not modify the concentrations of brain noradrenaline (NA) or acetylcholine, which are respectively reduced and increased by dextroamphetamine. Amineptine did not affect significantly the decrease of brain NA induced by an intraventricular injection of 6-hydroxydopamine (6-OHDA), an effect significantly antagonized by dextroamphetamine. Like amphetamine, amineptine significantly reduced the effect of 6-OHDA on brain dopamine. Both drugs increased the striatal concentrations of homovanillic acid and showed a cross-tolerance in this action. It is suggested that both drugs may act similarly on the striatal dopaminergic system and that amineptine appears to be a new type of antidepressant with a brain biochemical profile differing from that of other antidepressant drugs. 28 references. (Author abstract modified)

001237 Scatton, Bernard; Bischoff, Serge; Dedek, Jaroslav; Korf, Jakob. Synthelabo, Dept. of Biology, 31, av. P.V. Couturier, 92220 Bagneux, France **Regional effects of neuroleptics on dopamine metabolism and dopamine-sensitive adenylate cyclase activity.** European Journal of Pharmacology (Amsterdam). 44(4):287-292, 1977.

The effect of haloperidol, chlorpromazine, thioridazine and sulpiride on the levels of dihydroxyphenylacetic acid and homovanillic acid, as an index of dopamine (DA) turnover, and on the activity of DA stimulated adenylate cyclase was investigated in the striatum, the nucleus accumbens and the tuberculum olfactorium of the rat brain. Haloperidol, chlorpromazine and thioridazine caused a more marked increase in DA turnover in the striatum than in the mesolimbic areas, while the reverse was true for sulpiride. In contrast, although the relative potency of these compounds varied greatly, the Ki of each drug for the DA sensitive adenylate cyclase was similar in these three structures of rat brain. The results indicate that in the three brain structures investigated there was no correlation between the differential effects of neuroleptics on dopamine turnover in vivo and the blockade by these drugs of the DA sensitive adenylate cyclase activity in vitro. 30 references. (Author abstract)

001238 Sesawa, Tomio; Nakata, Yoshihiro; Yajima, Haruaki; Kitagawa, Kouki. Hiroshima University School of Medicine, Hiroshima 734, Japan **Further observation on the lack of active uptake system for substance p in the central nervous system.** Japanese Journal of Pharmacology (Kyoto). 27(4):573-580, 1977.

Crude mitochondrial P2 fractions from bovine hypothalamus and substantia nigra, slices from rabbit spinal cord and mesencephalon and glial fractions from rabbit brain were incubated with (3H)-substance-P and the uptake was measured and compared with those for 5-HT and GABA. Substance-P was to some extent taken up into the fractions but this uptake was neither temperature nor time dependent and the pellet/medium ratios were less than 1. Similar results were obtained in high potassium treated slices from rabbit mesencephalon. The rate of uptake for (3H)-subsstance-P increased linearly in proportion to the medium concentration, suggesting a nonsaturable binding. These results, together with previous observations provide strong evidence that nerve terminals and glial cells lack a temperature sensitive, active uptake system capable of terminating transmitter action of substance P at the synapse. 17 references. (Author abstract)

001239 Sethy, V. H.; Solomon, C. A. Upjohn Company, Kalamazoo, MI 49001 **Effects the hypnotics and antianxiety drugs on acetylcholine (ACh) concentrations in discrete areas of the rat brain.** Pharmacologist. 19(2):234, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of several CNS depressants on acetylcholine (ACh) concentrations in discrete regions of the rat brain was reported. Pentobarbital, chloral hydrate, and meprobamate significantly increased ACh concentrations in the cerebral cortex, striatum, hippocampus, and brainstem. Diazepam, flurazepam, and triazolam significantly increased ACh concentrations in only the cerebral cortex and striatum. Alprazolam and ketazolam had no significant effect on regional ACh concentrations. It is suggested that pentobarbital, chloral hydrate, and meprobamate may produce nonspecific depression in the activity of the whole central nervous system, whereas benzodiazepines may have specific effects on certain areas of the brain. (Author abstract modified)

001240 Shah, Nandkumar S.; Gulati, O. D.; Powell, D. A.; Kleinburd, Vicki. VA Hospital, Columbia, SC 29201 **Regional localization of (14C)Mescaline in rabbit brain after intraventricular administration: effects of chlorpromazine and iproniazid pretreatment.** Neurochemical Research. 2(3):265-279, 1977.

To obtain clues regarding the site and mode of action of mescaline, the regional distribution of mescaline-C14 in rabbit brain after its intraventricular injection is attempted, after pretreatment with chlorpromazine and iproniazid. The distribution of mescaline-C14 and its deaminated metabolite trimethoxyphenylacetic-C14 acid (TMPA) in 12 brain regions was examined at 15, 60, and 180 minutes after injections. Radioactivity reached peak levels within 15 minutes. The spinal cord, superior colliculus, pons, hypothalamus, caudate, medulla oblongata, and inferior colliculus contained 23 to 57 nmol/g of mescaline; the thalamus, tegmentum, and cerebellum, 12-15 nmol/g; and the cerebrum and hippocampus, less than 10 nmol/g; the levels of TMPA ranged from 0.5to 5 nmol/g. The levels of mescaline and of TMPA in all brain areas were considerably decreased 180 min after its injection. Pretreatment with chlorpromazine (CPZ) lowered mescaline concentrations in the hippocampus, caudate, thalamus, and cerebrum and elevated them in the spinal cord, medulla oblongata, pons, and tegmentum; TMPA levels as the percentage of total radioactivity were not affected. Pretreatment with iproniazid uniformly reduced the TMPA levels in all brain areas, with the resultant increases in mescaline levels. Chlorpromazine's effect in lowering the mescaline concentrations in the areas belonging to the limbic system may have significance in explaining its antihallucinogenic effect in humans and its ability to block the altered behavior induced by the latter drug in laboratory animals. 49 references. (Author abstract modified)

001241 Sharifi Hossaini, Khadijeh. West Virginia University, Morgantown, WV **Involvement of brain cyclic AMP in morphine tolerance and physical dependence. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. Mfilms, No. 77-22737 HC$15.00 MF$7.50 207 p.

To investigate the possible role of brain adenosine 3',5'-monophosphate (cAMP) in the mediation of morphine tolerance and dependence, a series of in vivo and in vitro studies were undertaken in the rat. Administration of cAMP antagonizes the analgesic response of morphine in tolerant and nontolerant rats and accelerates the development of induced morphine tolerance. Treatment of rats daily with cAMP during dependence and withdrawal markedly reduces high voltage EEG slow bursts, and enhances behavioral hyperarousal, thus enhancing development of physical dependence. Pargyline potentiates the accelerating effect of cAMP on tolerance development but does not alter cAMP effects on physical dependence. Finally, alpha-methylparatyrosine inhibits cAMP acceleration of tolerance, but does not modify cAMP effects on physical dependence. Results strongly suggest an involvement of brain cAMP in the mediation of central morphine effects, and provide preliminary evidence for some cAMP interaction with biogenic amines. (Journal abstract modified)

001242 Shater, H. A. O.; Pleuvry, Barbara J. Dept. of Pharmacology, Stopford Building, University of Manchester, Oxford Rd., Manchester M13 9PT, England **A sex difference in the interaction between promethazine and morphine in the mouse.** Journal of Pharmacy and Pharmacology (London). 29(10):612-615, 1977.

The effects of promethazine on the antinociceptive and respiratory actions of morphine are examined in the mouse. Moderate doses of promethazine potentiated morphines action in male mice but inhibited it in female mice. Gonadectomy abolished the interaction between promethazine and morphine in both sexes, although the intensity and duration of morphine's activity was greatly enhanced in these mice. Replacement of estradiol in ovariectomized mice restored morphine's activity to intact female control values. Interactions between promethazine and morphine, however, required progesterone, as well as estradiol, replacement to obtain results approaching those obtained in intact female mice. It is suggested that the rate of morphine's metabolism in the normal adult mouse may be enhanced by circulating sex hormones; and removal of these hormones might then revert the rate of morphine's metabolism to a slower basal rate. 10 references. (Author abstract modified)

001243 Shinohara, Yukito; Sakai, Fumio; Ishihara, Tadayuki; Kobatake, Keitaro; Nakahara, Katsuhiko; Gotoh, Fumio. Department of Neurology, Tokai University, Japan **Nonparticipation of cholinergic mechanism in chemical control of cerebral vasomotor activity.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):300-301, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, the contribution of cholinergic nervous mechanism to the chemical control of cerebral vasomotor activity was studied in 24 adult cats anesthetized with urethane and chloralose. Cerebral blood flow, arterial oxygen, arterial carbon dioxide, acidity, and blood pressure were determined during each procedure. Intravenous administration of the anticholinergic drug atropine slightly decreased cerebral blood flow, but an increase in blood flow by inhalation of CO2 was not influenced. It was concluded that cholinergic innervation has a functional influence in the regulation of cerebral blood flow, but not a direct influence on the mechanism of chemical control. 5 references.

001244 Sjogren, C. Research Laboratories, AB Leo, Helsingborg, Sweden **Alpha-adrenoceptor blockade by tricyclic antidepressants.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):75, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, alpha-adrenoceptor blockade by tricyclic antidepressants were studied in cats and rats in vivo in an attempt to determine the pharmacological basis of the development of hypotension in some patients treated with the antidepressants. The electrically stimulated nictitating membrane in the cat and phenylephrine induced blood pressure rises in the rat were used as indications of alpha-adrenoceptor stimulatory response. Lofepramine potentiated but desipramine and imiparamine inhibited contractions in the nictitating membrane. The three compounds decreased the blood pressure rises but lofepramine produced the weakest effect. In experiments which included influence on increasing stimulatory frequencies on the nictitating membrane and increasing doses of phenylephrine, the effects of the compounds appeared to be competititve.

001245 Smith, Carol Grace; Smith, Michael, T.; Besch, Norma F.; Buoy, M. Elizabeth. Departments of Pharmacology and Pathology, University of Texas Health Science Center, San Antonio, TX **The effect of chronic administration of tetrahydrocannabinol (THC) on the secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH) in the ovariectomized rhesus monkey.** Pharmacologist. 19(2):219, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of acute and chronic administration of delta9-tetrahydrocannabinol (THC) on the secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH) in ovariectomized Rhesus monkeys was reported. Significant changes in blood levels of LH and FSH were measured 6 hr following acute administration of 0.625mg/kg or 1.25mg/kg THC. Neither of these doses of THC caused a significant change in LH or FSH levels during 14 da of chronic administration. (Author abstract modified)

001246 Smith, P. Blaise; Appel, S. H. Department of Biochemistry, Bowman Gray School of Medicine of Wake Forest University, Winston Salem, NC 27103 **Development of denervation alterations in surface membranes of mammalian skeletal muscle.** Experimental Neurology. 56(1):102-114, 1977.

The effect of denervation on selected biochemical properties of mammalian skeletal muscle surface membranes on rats was studied. Studies were performed on muscle denervated 1, 2, 3, 5, or 7 days. Plasma membrane (sarcolemma) and membrane tentatively identified as transverse tubule were isolated. After denervation the surface membranes of skeletal muscle underwent specific biochemical alterations without gross changes in membrane polypeptide or lipid composition. Seven days after denervation sarcolemmal membranes underwent a slight density shift. Na, K(Mg) ATPase activity and sialic acid content increased beginning 3 days postdenervation. Basal, sodium fluoride stimulated, and isoproterenol stimulated adenyl cyclase activity decreased 50% after 5 days of denervation. Isoproterenol stimulated activity was enhanced by 5'-guanylyl imidodiphosphate. Membrane tentatively identified as transverse tubule increased in yield as denervation progressed. In this fraction endogenous protein kinase activity for a 28,000 MW polypeptide decreased by 50% between days 2 and 3. The decrease in membrane protein phosphorylation was paralleled by a decrease in content of the 28,000 MW polypeptide. These experiments add to physiological and morphological studies on denervation induced alterations of skeletal muscle structure and function. 35 references. (Journal abstract modified)

001247 Smith, Peter G. Dept. of Zoology, University of Liverpool, Liverpool L69 3BX, England **The effect of chlorpromazine on cell membrane resistance and capacitance.** European Journal of Pharmacology (Amsterdam). 45(3):251-256, 1977.

The effects of chlorpromazine on cell membrane resistance and capacitance were investigated using isolated frog skin. Chlorpromazine caused rises in the p.d. across the skin, and decreased membrane capacitance by up to 5%. Resistance was decreased by up to 25%. The effects on p.d. and resistance were obtained only when the drug was added to the solution bathing the outside of the skin. It is suggested that these effects may be caused by increases in the sodium permeability of the outer membrane. The decrease in capacitance is not consistent with an increase in membrane area without changes in thickness or permittivity. It is suggested that the decrease in capacitance may be due to a loss of water from the membrane. 24 references. (Author abstract modified)

001248 Smith, Thomas L. Dept. of Biological Chemistry, Harvard Medical School, Belmont, MA 02178 **Increased synthesis of striatal dopamine by N,N-dimethyltryptamine.** Life Sciences (Oxford). 21(11):1597-1602, 1977.

The effect of acute doses of N,N-dimethyltryptamine (DMT) on the synthesis or degradation rates of rat diencephalon norepinephrine and striatal dopamine was estimated by administering 150microcuries L-tyrosine-3,5-3H at various times before sacrifice. In all cases DMT, 20mg/kg, was injected one half hour before sacrifice. In both acute and chronically treated rats, an increase in endogenous levels of 3-methoxytyramine was observed, while no effect was observed in the diencephalon adrenergic system. The results suggest that DMT increases central dopamine turnover. 21 references. (Author abstract)

001249 Stanishevskaya, A. V.; Mezentseva, L. N. Lab. psikhofarm., Institute sudebnoy psikhatrii im. prof. V. P. Serbskogo, Ministerstva zdravookhraneniya SSSR, Moscow, USSR **/Effect of certain psychopharmacological agents on adaptation under stress./** Vliyanie nekotorykh psikhofarmakologicheskikh preparatov na adaptatsiyu v usloviyakh stressa. Farmakologiya i Toksikologiya (Moskva). 40(1):9-12, 1977.

A study of the effect of esduxen, L-dopa, and pyroxan on adaptation under stress induced by electric shock in immobilized rats is reported. Results demonstrated that the development of pathological mental states caused by psychophysiological stress and accompanied by development of ulcerative lesion of the gastric mucosa are associated with the degree of drop in catecholamine level in the mesencephalon and hypothalamus. Administration of seduxen and L-dopa in combination with seduxen, or seduxen plus the L-adrenoblocking agent pyrosan reduced the incidence of gastric ulcer. The protective effect of the L-dopa/pyroxan combination was eliminated by additional administration of the beta adrenoblocking agent inderal. 8 references. (Journal abstract modified)

001250 Stanley, Michael; Wilk, Sherwin. Dept. of Pharmacology, Mt. Sinai School of Medicine, CUNY, Fifth Ave. & 100th St., New York, NY 10029 **The effect of antipsychotic drugs and their clinically inactive analogs on dopamine metabolism.** European Journal of Pharmacology (Amsterdam). 44(4):293-302, 1977.

Changes in dopamine metabolite levels in the rat striatum and tuberculum olfactorium following the administration of three nonantipsychotic butyrophenones and a nonantipsychotic benzazepine were compared to the effects seen following the antipsychotics haloperidol, chlorpromazine and clozapine. The nonantipsychotics, although clinically ineffective, were reported as active in a variety of animal screening tests. Haloperidol, chlorpromazine and clozapine produced a dose dependent increase in 3,4-dihydroxyphenylacetic acid (DOPAC) levels in both regions. Of the nonantipsychotic drugs only one significantly elevated the level of DOPAC. It is concluded that the dose dependent elevation of DOPAC in the striatum and tuberculum olfactorium of the rat is a good predictor of antipsychotic efficacy. 46 references. (Author abstract modified)

001251 Steranka, Larry; Sanders-Bush, Elaine. Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN **Temporal effects of p-chloroamphetamine on catecholamine synthesis.** European Journal of Pharmacology (Amsterdam). 45(1):83-86, 1977.

To determine whether p-chloroamphetamine (PCA) induces time dependent biphasic changes in catecholamine synthesis, in vivo synthesis rates of endogenous norepinephrine (NE) and dopamine (DA) in rats were estimated, and radioactive tyrosine and NE and DA were determined at varying times in vitro. Data indicate that within 15 min after administration of PCA the conversion index of both NE and DA was increased.

The effect on DA synthesis was similar, but of less magnitude after 1.25 h, while the effect on NE was reversed, i.e. the conversion index of both NE and DA was decreased. This biphasic effect of PCA on NE synthesis is discussed in the context of two opposing regulatory mechanisms for neuronal catecholamine synthesis. 11 references. (Author abstract modified)

001252 Strahlendorf, Jean R.; Goldstein, Frederick J. Department of Biological Sciences, Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104 **Central antagonism of tyramine-induced systemic hypotension by mescaline.** Journal of Pharmacy and Pharmacology (London). 29(11):699-700, 1977.

Central antagonism of tyramine induced systemic hypotension by mescaline was studied in rabbits to further examine the premise that psychotomimetic agents such as mescaline modify biogenic amine concentrations in CNS. To examine the hypothesis that mescaline elicits central catecholaminergic antagonism, the interaction of mescaline with endogenously released noradrenaline was observed. Centrally initiated changes in systemic blood pressure provided a means of assessing mescaline activity. Within 5 minutes of injection, mescaline reversed tyramine induced hypotension in subjects, elevating mean systemic arterial pressure by 43%. The mechanism of action of mescaline is discussed in light of the evidence gained. 17 references. (Author abstract modified)

001253 Stramentinoli, G.; Catto, E.; Algeri, S. Department of Biochemistry, BioResearch, I-20060 Liscate, Milano, Italy **The increase in S-adenosyl-L-methionine (SAMe) concentration in rat brain after its systematic administration.** Communications in Psychopharmacology. 1(2):89-97, 1977.

The effect of the systematic administration of S-adenosyl-L-methionine (SAMe) on the concentration of SAMe in rat brain was measured in an experiment in which male rats received intravenous injections of radiolabelled SAMe. Previous experiments with tracer doses of radiolabelled SAMe had shown poor absorption of this substance into the brain. Also, administration of labelled methionine, the aminoacid precursor of SAMe, proved more efficient in increasing SAMe levels in brain. The present study shows that 0.25mmoles/Kg of intravenously injected SAMe can increase brain levels of this cofactor as much as 50% of the basal levels. A close correlation between plasma and brain levels is also shown. The amount of SAMe passing through the blood-brain barrier represents, however, only a small fraction of the circulating cofactor. Brain SAMe levels are demonstrated to be higher after intravenous administration of exogenous SAMe than after an equimolar dose of methionine. 10 references. (Author abstract modified)

001254 Sundquist, Hannu; Anttila, Markku; Nieminen, Lauri; Urpo, Kaarina; Kalliomaki, Lennart. Research Center Laake-Medipolar, SF-20101 Turku 10, Finland **The effect of dihydroergotoxine on the adenylate cyclase activity in homogenates of rat cerebral cortex.** Acta Pharmacologica et Toxicologica (Kobenhavn). 40(5):589-592, 1977.

The effect of dihydroergotoxine, which has been reported to be clinically beneficial in age induced cerebral dysfunction in humans, on the fluoride stimulated adenylate cyclase activity of rat cerebral cortex was studied in vivo and in vitro. The drug markedly inhibited response to fluoride by adenylate cyclase in vitro and produced a significant decrease in cyclic adenosine 3',5'-monophosphate (cAMP) in vivo. The clinical significance of this effect cannot be determined until the relationship between cAMP levels and clinical disturbances in brain function has been elucidated. 15 references.

001255 Tache, Yvette; Du Ruisseau, Pierre; Ducharme, Jacques-Raymond; Collu, Robert. Universite de Montreal, Montreal, Quebec, Canada **Antagonism of pentobarbital-induced hormonal changes by TRH in rats.** European Journal of Pharmacology (Amsterdam). 45(4):369-376, 1977.

In a study of antagonism of pentobarbital induced hormonal changes by thyrotropin releasing hormone (TRH), in adult male rats, injection of TRH into a lateral ventricle of the brain 5 min prior to pentobarbital (PB) administration, a significant dose related inhibition of prolactin (PRL) release was caused in doses ranging from 500 to 5ng. Among eight TRH analogues devoid of thyrotropin releasing activity, six were found to significantly suppress PB induced PRL secretion at an intraventricular dose level of 10 micrograms, and the three most effective in this respect were also able to counteract growth hormone (GH) release elicited by PB. TRH did not affect the increase of plasma PRL induced by acute stress. P-Chlorophenylalanine (PCPA) completely blocked the antagonistic effect of TRH on all PB induced hormonal changes, suggesting that serotoninergic mechanisms may be involved in the extrapituitary effects of TRH. 33 references. (Author abstract modified)

001256 Takagi, Hiroshi; Satoh, Masamichi; Akaike, Akinori; Shibata, Takashi; Kuraishi, Yasushi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan **The nucleus reticularis gigantocellularis of the medulla oblongata is a highly sensitive site in the production of morphine analgesia in the rat.** European Journal of Pharmacology (Amsterdam). 45(1):91-92, 1977.

To determine the effect of microinjection of morphine into the nucleus reticularis gigantocellularis (NRGC) of the medulla oblongata on the behavioral nociceptive response, a series of experiments were undertaken in the rat. Injection of morphine into the NRGC produced antinociceptive effects in a dose dependent manner. Analgesic effect reached its maximum peak within 1 min at all three dosages tested and disappeared after 30 to 90 min. No antinociceptive action was produced by microinjections of morphine into the periaqueductal gray matter, the nucleus raphe magnus, the nucleus reticularis lateralis, the nucleus reticularis pontis caudalis, or the nucleus reticularis ventralis. It is suggested that the NRGC may play an important role in the mediation of morphine induced analgesia after systemic injection. 4 references.

001257 Thomas, P. C.; Jones, R. B. Welsh School of Pharmacy, UWIST, King Edward VII Avenue, Cardiff, Wales **The effects of clomipramine and desmethylclomipramine on the in vitro uptake of radiolabelled 5-HT and noradrenaline into rat brain cortical slices.** Journal of Pharmacy and Pharmacology (London). 29(9):562-563, 1977.

The effects of clomipramine and of desmethylclomipramine on the in vitro uptake of radiolabeled 5-HT and NA into rat brain cortical tissue slices were examined to determine if there were significant differences in the activities of the parent compound and its metabolite. Desmethylclomipramine was less active than clomipramine as an inhibitor of 5-HT uptake but was more potent as an inhibitor of NA uptake. It is suggested that desmethylclomipramine may contribute to the overall antidepressant effect of clomipramine in man and that care should be exercised when regarding clomipramine as a pharmacological tool with relatively specific 5-HT uptake blocking activity. 8 references.

001258 Thyberg, Johan; Axelsson, Jan Erik; Hinek, Aleksander. Department of Histology, Karolinska Institutet, S-10401, Stockholm, Sweden **In vitro effects of chlorpromazine**

on microtubules and the Golgi complex in embryonic chick spinal ganglion cells: an electron microscopic study. Brain Research (Amsterdam). 137(2):323-332, 1977.

To examine the in vitro effects of chlorpromazine (CPZ) on microtubules and the Golgi complex, spinal ganglia from 11-day-old chick embryos were incubated in media containing CPZ, lidocaine, or d-amphetamine and subsequently examined by transmission electron microscopy. CPZ and lidocaine both caused a structural modification of the neuroblasts similar to that induced by the microtubular disrupting drugs colchicine and vinblastine. That is, there was a partial disappearance of cytoplasmic microtubules with a concomitant increase in the number of microfilaments and dictyosomes of the Golgi complex changed, with the number of narrow cisternae decreasing and the number of associated vacuoles increasing. Moreover, the dictyosomes were more distinctly separated from each other than in control ganglia. d-Amphetamine did not give rise to any clear changes in either the microtubular system or the Golgi complex and, furthermore, opposed the colchicine like effects of CPZ. On the basis of these results it is suggested that the subcellular mechanism of action of CPZ involves the cytoplasmic microtubular system and thus secondarily leads to structural and functional alterations in the Golgi complex, viz.,in the case of nerve cells, a disturbance in the production and packaging of material destined for the axon terminals. 24 references. (Author abstract modified)

001259 Tjioe, Sarah A. Ohio State University Research Foundation, Department of Pharmacology, 1314 Kinnear Rd., Columbus, OH 43212 **Phenothiazine metabolites as mitochondrial inhibitors.** Research Report, NIMH Grant MH-23805, 1977. 11 p.

The mechanisms by which hydroxylated phenothiazine metabolites inhibit calcium accumulation and respiration in preparations of isolated rat brain mitochondria are explored. In isolated brain mitochondria allowed to accumulate calcium, with adenosine triphosphate as substrate, exposure to 7,8-dihydroxychlorpromazine (7,8-diOH-CPZ) produced delayed but complete release of the cation. This was accompanied by marked swelling of mitochondria. Glutamate supported respiration and oxidative phosphorylation were also blocked, but with very little change in the ultrastructure of the mitochondria. Resuspending the mitochondria in fresh medium did not allow respiration to resume, suggesting that the inhibition is not readily reversible. 2,3-Dihydroxypromazine was as effective as 7,8-diOH-CPZ in blocking glutamate supported respiration and oxidative phosphorylation; however, it did not affect mitochondrial calcium uptake or retention. The addition of dithiothreitol, a sulfhydryl reducing agent, delayed the effects of 7,8-diOH-CPZ on calcium retention and oxidative phosphorylation, suggesting that 7,8-diOH-CPZ or one of its oxidation products may inhibit action at sulfhydryl sites. 7,8-Dioxo-CPZ had the same effects as the dihydroxy compound, indicating that oxidation products are inhibitory. Creatinephosphokinase, an enzyme thought to have a sulfhydryl group at its active site, was inhibited by 7,8-diOH-CPZ. It is suggested that oxidation products of hydroxylated phenothiazine metabolites and sulfhydryl inactivation may be involved in the effects of these compounds on calcium accumulation and respiration in mitochondria. (Author abstract modified)

001260 Tolbert, Lelland; Thomas, Thomas N.; Middaugh, Lawrence D.; Zemp, John W. Department of Biochemistry, Medical University of South Carolina, Charleston, SC 29403 **Ascorbate attenuates apomorphine-induced hypothermia in vivo.** Pharmacologist. 19(2):155, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of ascorbate on the induction of hypothermia by the dopamine (DA) agonist apomorphine in mice was reported. Rectal temperatures were reduced after apomorphine. Ascorbate alone did not alter temperature but ascorbate injected prior to apomorphine significantly attenuated the apomorphine induced hypothermia at all times examined. It is suggested that ascorbate, which has previously been found to inhibit DA binding to its receptor and to inhibit the DA stimulation of striatal adenylate cyclase in vitro, may block the binding of apomorphine to the DA receptor. A potential therapeutic role for ascorbate as a blocking agent for dopaminergic transmission is also suggested. (Author abstract modified)

001261 Torronen, Riitta; Nousiainen, Unto; Marselos, Marios. Dept. of Physiology, University of Kuopio, SF-70101 Kuopio 10, Finland **Inducible aldehyde dehydrogenases in the hepatic cytosol of the rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(3):263-272, 1977.

The effects of phenobarbital on aldehyde dehydrogenase activity in the rat were investigated. Phenobarbital produced a uniform induction of aldehyde dehydrogenase in all rats, when measured with micromolar substrate concentration. The inducible low Km enzyme of the cytosol is not genetically determined like the high Km enzyme, and shows a wide specificity for aliphatic as well as for aromatic aldehydes. Despite the inducibility of the cytosolic enzymes, no alterations were found in the mitochondrial aldehyde dehydrogenase activities after phenobarbital treatment. The oxidation of D-glucuronolactone takes place only in the cytosol, seems to be dependent on the low Km aldehyde dehydrogenase, is enhanced by phenobarbital in all rats without a genetic predisposition, and has a dose response curve similar to that of the low Km aldehyde dehydrogenase. 28 references. (Journal abstract)

001262 Trulson, M. E.; Ross, C. A.; Jacobs, B. L. Department of Psychology, Green Hall, Princeton University, Princeton, NJ 08540 **Lack of tolerance to the depression of raphe unit activity by lysergic acid diethylamide.** Neuropharmacology (Oxford). 16(11):771-774, 1977.

The responsiveness of serotonin containing midbrain raphe neurones to lysergic acid diethylamide (LSD) was examined in rats made tolerant to LSD by its repeated administration. No significant changes in the dose/response relationships between raphe unit activity and LSD administration were observed following chronic administration of low or high doses of LSD. Similarly, no significant change was observed when rats were pretreated with LSD every 6 hr for 4 days. In addition, no signficant changes in spontaneous raphe unit activity nor duration of LSD induced depression of unit activity occurred following chronic LSD pretreatment. These data suggest that the dramatic tolerance which develops to LSD on behavioral tests is not mediated by a change in the sensitivity of serotonin containing neurons to LSD. 20 references. (Author abstract)

001263 Trush, Michael A.; Van Dyke, Knox; Wilson, Mark E.; Reasor, Mark J. Dept. of Pharmacology, West Virginia University, Morgantown, WV 26506 **Chemiluminescence resulting from an interaction between imipramine and human polymorphonuclear leukocytes.** Research Communications in Chemical Pathology and Pharmacology. 18(4):645-664, 1977.

The addition of imipramine to a suspension of resting polymorphonuclear leukocytes (PMNs) resulted in the generation of chemiluminescence (CL). In the presence of a particle

(zymosan) capable of activating the PMNs to generate reactive oxygen species, the magnitude of CL observed with imipramine was greatly enhanced. No CL was detected upon the addition of imipramine to PMNs isolated from a chronic granulomatous child or to alveolar macrophages isolated from rats. Another tricyclic antidepressant, amitriptyline, failed to generate CL with PMNs either alone or in the presence of zymosan; however, both imipramine and amitriptyline generated CL upon addition to the xanthine oxidase purine superoxide generating system. Although the mechanism by which this drug/cell interaction results in the generation of CL is not known, the observations are suggestive that the CL may originate, in part, from the activation of imipramine by some reactive oxygen state(s). 3 references. (Author abstract)

001264 Trzcinka, G. P.; Lipton, J. M.; Hawkins, M.; Clark, W. G. Dept. of Psychiatry, University of Texas Health Science Center at Dallas, Dallas TX 75235 **Effects on temperature of morphine injected into the preoptic/anterior hypothalamus, medulla oblongata, and peripherally in unrestrained and restrained rats.** Proceedings of the Society for Experimental Biology and Medicine. 156(3):523-526, 1977.

Effects on temperature of morphine injected into the preoptic/anterior hypothalamus (PO/AH), medulla oblongata (MED), and peripherally in unrestrained and restrained rats were studied. Changes in rectal temperatures were determined in unrestrained rats after injections of morphine into the PO/AH and MED regions. Injections into the former site consistently caused hyperthermia, while medullary injections caused only inconsistent small responses. Destruction of the PO/AH region did not enhance the response to medullary injections of morphine. Restraint reversed responses to PO/AH and i.p. administration of morphine, resulting in hypothermia. Results provide additional evidence for the concept of a sensitive primary temperature control in the PO/AH region and a secondary control, which responds minimally to drugs, in the medulla. 17 references (Author abstract)

001265 Tsuchiya, Toshiro; Fukushima, Hideaki. Research and Development Center, Pharmaceuticals Div., Sumitomo Chemical Co, 4-2-1, Takatsukasa, Takarazuka, Hyogo 665, Japan **Effects of benzodiazepines on PGO firings and multiple unit activity in the midbrain reticular formation in cats.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 43(5):700-706, 1977.

Effects of benzodiazepines administered by the intraperitoneal route on pontogeniculooccipital (PGO) firings and multiple unit activity in the midbrain reticular formation in chronic cat preparations were investigated at various levels of consciousness. Changes in the sleep-wakefulness cycle induced by direct injection of benzodiazepines into the reticular formation were also investigated. Benzodiazepines markedly decreased multiple unit activity in the midbrain reticular formation during each stage of sleep, but had little effect during behavioral and EEG arousal. Benzodiazepines did not affect PGO firing rate, but attenuated all increase of multiple unit activity following PGO firings. The bilateral injection of benzodiazepines into the midbrain reticular formation induced an increase of arousal and a decrease of slow-wave sleep, but did not change the amount of paradoxical sleep. It is concluded that benzodiazepines show a mixture of depressant and facilitatory effects which seem to vary with the state of consciousness of the animal. 29 references.

001266 Tucker, Anne N.; Friedman, Marvin A. Department of Pharmacology, Medical College, Health Sciences Division, Virginia Commonwealth University, Richmond, VA 23298 **Effects of cannabinoids on L1210 murine leukemia: 1. inhibition of DNA synthesis.** Research Communications in Chemical Pathology and Pharmacology. 17(4):703-714, 1977.

The effect of cannabinoid derivatives on thymidine-3H uptake in L1210 murine leukemia was determined. In experiments at 200mg/kg 3 hrs after treatment, the descending order of activity was delta9-tetrahydrocannabinol cannabinol, cannabidiol, abnormal cannabidiol, 11-hydroxy-tetrahydrocannabinol, delta8-tetrahydrocannabinol. The inhibitory effect of delta8-tetrahydrocannabinol was 99%. When animals were dosed on consecutive days with delta9-tetrahydrocannabinol and killed on the third day, thymidine-3H incorporation was increased while delta9-tetrahydrocannabinol retained its inhibitory activity under the same conditions. Delta9-tetrahydrocannabinol and delta8-tetrahydrocannabinol inhibited RNA and protein synthesis in a fashion analagous to the inhibition of DNA synthesis. 13 references. (Author abstract)

001267 Urca, Gideon; Frenk, Hanan; Liebeskind, John C; Taylor, Anna N. Department of Psychology, University of California, Los Angeles, CA 90024 **Morphine and enkephalin: analgesic and epileptic properties.** Science. 197(4298):83-86, 1977.

The effects of systemic and intracerebroventricular administration of morphine and enkephalin on periaqueductal gray matter multiple unit firing and neural activity were examined in rats. Systemic and intracerebroventricular administration of analgesic doses of morphine resulted in large increments of spontaneous multiple unit activity in the periaqueductal gray matter of the awake rat. Intracerebroventricular injection of methionine enkephalin gave analgesia in only eight of 19 rats, but in all eight and in no others, increased periaqueductal multiple unit firing was also seen. These findings support the view that the periaqueductal gray matter is actively involved in endogenous mechanisms of analgesia. A striking observation was that enkephalin caused electrographic and behavioral epileptic phenomena in most animals. This observation together with other recent findings suggests that endogenous enkephalin may play some role in epileptogenesis. 19 references. (Author abstract modified)

001268 Uretsky, Norman J.; Kamal, Linda; Snodgrass, S. Robert. Department of Neuroscience, Children's Hospital Medical Center, Boston, MA 02115 **Role of calcium in the amphetamine-induced stimulation of catechol formation in the striatum.** Pharmacologist. 19(2):195, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the role of calcium (Ca) in the amphetamine induced stimulation of radiolabeled catechol formation from radiolabeled tyrosine in striatal slices and in synaptosomes was reported. In striatal slices, amphetamine produced a 193% increase in catechol formation in the presence of Ca compared to a 14% increase in the presence of EGTA but no Ca. The stimulation of catechol synthesis was reduced in the presence of magnesium, manganese, and verapamil, suggesting that the stimulation was related to an increased entry of Ca into dopamine nerve terminals. Catechol synthesis in synaptosomes differed from that in tissue slices in that: 1) Ca did not inhibit basal catechol synthesis; 2) the magnitude of the amphetamine induced stimulation was less; 3) amphetamine induced stimulation was less dependent on the Ca concentration; and 4) the amphetamine induced stimulation was not reduced by high magnesium or verapamil concentrations. It is suggested that amphetamine

can stimulate catechol synthesis by both Ca dependent and Ca independent processes; in tissue slices, the Ca dependent process is greater while in the synaptosomes, the Ca independent process appears more significant. (Author abstract modified)

001269 Van Loon, Glen R.; Kim, Chul. Dept. of Medicine, Clinical Science Division, University of Toronto, Toronto M5S 1A8, Canada **Effect of beta-endorphin on striatal dopamine metabolism.** Research Communications in Chemical Pathology and Pharmacology. 18(1):171-174, 1977.

Acute intraventricular administration of human beta-endorphin increased 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) concentrations in rat striatum at a time when the catatonic effect was also present. This effect of beta-endorphin is compatible with increased striatal dopamine turnover and is similar to the effect noted previously with morphine administration. 8 references. (Author abstract)

001270 van Ree, Jan M. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, Utrecht, The Netherlands **Multiple brain sites involved in morphine antinociception.** Journal of Pharmacy and Pharmacology (London). 29(12):765-767, 1977.

To localize the antinociceptive effect of morphine in rat brain, various brain sites were mapped for antinociceptive activity by unilateral injection of morphine and response latency was determined; and nociceptive response of rats was assessed following injection of various dosages of morphine injected into various parts of the brain ventricle system. A marked antinociceptive effect was found when morphine was injected in or near the ventricles, substantia grisea centralis, lemniscus medialis, and the nucleus mediodorsalis thalami; and moderate activity was found in the formation reticularis, nucleus lateralis septi, the nuclear posterior and anterior hypothalami, nucleus mamillaris lateralis, and the superior and inferior colliculus. In general, peak activity occurred 40 min after injection. Morphine injections to the fourth ventricle were more effective in producing analgesia than those into other parts of the ventricular system. Results suggest that most of the active sites may be related to the extralemniscal somatosensory pathways. 11 references.

001271 Vance, M. A.; Ross, S. M.; Millington, W. R.; Blumberg, J. B. College of Pharmacy and Allied Health Professions, Northeastern University, Boston, MA 02115 **Cholinergic modification of the inhibition of dopamine (DA)-induced hyperactivity by neuroleptics.** Pharmacologist. 19(2):174, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of a cholinergic agonist, spiro-(1-methyl-4-piperidyl)-N-ethylsuccimide (RS-86) on dopamine (DA) induced hyperactivity in rats and on the inhibition of DA induced hyperactivity by neuroleptic drugs was reported. Direct bilateral application of DA to the nucleus accumbens of animals pretreated with pargyline produced a significant increase in locomotor activity compared to saline controls. Pretreatment with RS-86 did not appreciably alter the response to DA. However, RS-86 potentiated the inhibition of DA induced hyperactivity by chlorprothixene, fluphenazine, and thioridazine. RS-86 did not modify the action of clozapine, a neuroleptic which lacks behavioral and biochemical evidence of DA receptor blockade. RS-86 also potentiated the catalepsy, hypothermia, and inhibition of apomorphine induced stereotypy elicited by chlorprothixene. It is suggested that cholinergic modifications affect mesolimbic DA systems. The results support the hypothesis that the actions of clozapine on DA systems may differ from those of other neuroleptic drugs. (Author abstract modified)

001272 Vaught, Jeffry L.; Takemori, A. E. Department of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **Interactions of leucine and methionine enkephalin with morphine in vitro and in vivo.** Pharmacologist. 19(2):189, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the interactions between leucine enkephalin (LE) or methionine enkephalin (ME) with morphine in vitro and in vivo was reported. Using naloxone as the antagonist, a comparison of pA-2 values obtained from the guinea pig ileum longitudinal muscle preparation revealed that LE and ME can be classified as pure narcotic agonists. Pretreatment of the muscle strip with increasing concentrations of either LE or ME significantly increased the pA-2 value for morphine. Pretreatment with morphine significantly increased the pA-2 values for LE, ME, and morphine, but not nalorphine. The IC-50 for morphine was markedly decreased by pretreatment with LE. This potentiating effect was not exhibited by pretreatments with either ME or morphine. Intracerebroventricular or intraperitoneal administration of LE in mice prior to or after subcutaneous administration of morphine resulted in a significant, dose dependent decrease in the ED-50 of morphine in the tail flick assay while ME was without effect. It is suggested that LE and ME interact differently with morphine and that LE may be a potent modulator of morphine efficacy. (Author abstract modified)

001273 Vaupel, D. B.; Martin, W. R. National Institute on Drug Abuse Addiction Research Center, P.O. Box 12390, Lexington, KY 40511 **A comparison of the effects of 4-bromo-2,5-dimethoxyamphetamine (DOB), 3,4,5-trimethoxyamphetamine (TMA), para-methoxyamphetamine (PMA), d-amphetamine (A), and LSD in nontolerant and LSD tolerant chronic spinal dogs.** Pharmacologist. 19(2):230, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study comparing the effects of single doses of 4-bromo-2,5-dimethoxyamphetamine (DOB), 3,4,5-trimethoxyamphetamine (TMA), para-methoxyamphetamine (PMA), dextroamphetamine (A), and lysergic acid diethylamide (LSD) in nontolerant and in LSD tolerant chronic spinal dogs was reported. DOB and TMA markedly facilitated the flexor reflex, elicited stepping, increased the skin twitch reflex latency, and produced a modest mydriasis, whining, and tracking or staring. These effects are characteristic of LSD. A and PMA modestly facilitated the flexor reflex, produced marked mydriasis and bradycardia, and prolonged the skin twitch latency but did not elicit stepping. PMA did not evoke A-like stereotypy. All five drugs increased respiration and temperature. In spinal dogs made tolerant to LSD: 1) tolerance to the physiologic and behavioral effects of LSD developed; 2) cross-tolerance to all of DOB'S effects developed; 3) cross-tolerance developed to the physiologic and behavioral effects of TMA other than those on the pupils and the skin twitch reflex; and 4) no cross-tolerance to the effects of A or PMA developed. It is concluded that: 1) DOB has typical LSD-like properties; 2) PMA is primarily A-like; and 3) TMA is predominantly LSD-like but also has some A-like effects. (Author abstract modified)

001274 Volicer, L.; Puri, S. K.; Choma, P. Department of Pharmacology, Boston University School of Medicine, Boston,

MA 02118 **Cyclic GMP and GABA levels in rat striatum and cerebellum during morphine withdrawal: effect of apomorphine.** Neuropharmacology (Oxford). 16(11):791-794, 1977.

Cyclic GMP and GABA levels were measured in the striatum and cerebellum of naive rats and rats undergoing morphine withdrawal. Cyclic GMP levels were higher in rats sacrificed at 24 hrs and 72 hrs after the last morphine administration than in controls. GABA levels were lower in 24 hr withdrawn rats than in control and 72 hr withdrawn animals. Apomorphine increased cyclic GMP levels in both striatum and cerebellum to the same extent in controls and 72 hr withdrawn rats. In rats sacrificed 24 hrs after the last morphine dose apomorphine did not change the cyclic GMP level in the striatum while it was more potent in increasing the cyclic GMP level in the cerebellum. GABA levels were not affected by apomorphine treatment. 9 references. (Author abstract)

001275 Vyskocil, Frantisek. Institute of Physiology, Czechoslovak Academy of Science, Prague 4, Czechoslovakia **Diazepam blockade of repetitive action potentials in skeletal muscle fibres: a model of its membrane action.** Brain Research (Amsterdam). 133(2):315-328, 1977.

Using rat diaphragm muscle fiber and frog sartorius muscle fiber as models of an excitable membrane that allow an appropriate electrophysiological study, the effect of diazepam on individual action potentials (AP) and trains of impulses was measured by the intracellular microelectrode technique. In amounts comparable to those with a therapeutic effect, diazepam blocked trains of AP but single APs were not affected. Diazepam apparently increases the resting permeability of the muscle fibre membrane for chloride ions. In the presence of the drug, the higher permeability for Cl- diminishes the depolarization caused by the potassium released and accumulated in the vicinity of the membrane in the course of AP. The muscle fibre membrane thus does not respond by repetitive activity when partially depolarized and only one AP can be evoked when diazepam is present. It is suggested that similar changes in Cl- permeability may occur in brain excitable structures after diazepam administration and may account for some of the drug's therapeutic effects. 42 references. (Author abstract modified)

001276 Wallnau, Larry B. SUNY at Albany, Albany, NY **The psychopharmacology of morphine effects on tonic immobility. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-26523 HC$15.00 MF$8.50 92 p.

The psychopharmacology of morphine enhancement of tonic immobility (TI) was examined. The morphine effect on TI appears to be nonnarcotic since naloxone, a specific opiate antagonist, failed to block this effect. This finding is consistent with a midbrain/raphe model of TI and suggests that catecholminergic and cholinergic mechanisms do not participate in the morphine potentiation. Naloxone by itself did not affect TI, suggesting that TI is not homologous to endorphin induced catatonia. The effect of atropine on the morphine potentiation of TI remains inconclusive. Systemic and dietary manipulations of tryptophan failed to alter the morphine effects but pretreatment with PCPA, a selective depletor of serotonin, completely blocked the morphine enhancement. Dextrorphan, a nonnarcotic stereoisomer of the morphine agonist levorphanol, did not affect TI, a result that conflicts with a raphe model. Dextrorphan did elicit catalepsy in high doses, and this effect did not appear to be narcotic. (Journal abstract modified)

001277 Walter, Donald S.; Shilcock, Gillian M. Dept. of Pharmacology, Reckitt and Colman, Pharmaceutical Division, Damsom Lane, Hull HU8 7DS, England **Urinary 3-methoxy-4-hydroxyphenylglycol, an index of peripheral rather than central adrenergic activity in the rat.** Journal of Pharmacy and Pharmacology (London). 29(10):626-627, 1977.

Changes in urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) concentration when the central and/or peripheral noradrenaline metabolism is altered by the monoamine oxidase inhibitor nialamide are examined in rats. There were no changes in urinary MHPG when the drug was administered intracerebrally or intraperitoneally; but there was a significant decrease in brain MHPG 48 hrs after dosing. Both the urinary and brain MHPG concentrations of the intracerebroventricular control group were significantly greater than those of the intraperitoneal control group. It is suggested that in man the fraction of MHPG in the urine that originates from brain may be much larger than in the rat, thus allowing urinary MHPG to be used as an index of central noradrenergic activity. 13 references.

001278 Walters, J. R.; Lakoski, J. M.; Eng, N. NINCDS, National Institute of Health, Bethesda, MD 20014 **Effects of lergotrile (LER), an ergot derivative, on activity of substantia nigra pars compacta dopamine (DA) neurons.** Pharmacologist. 19(2):222, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a series of single unit recording studies on the effects of lergotrile, which has behavioral effects similar to those of apomorphine and which causes release of dopamine (DA) from synaptosomes, on the firing rates of DA neurons from the substantia nigra of anesthetized rats was reported. Intravenous injection of lergotrile caused a rapid, dose dependent, complete, haloperidol reversible inhibition of 63% of the DA neurons tested. The remaining cells were only partially inhibited. Intraperitoneal administration of lergotrile also caused inhibition of DA cells; 50% were completely inhibited. Unlike cells inhibited by apomorphine, lergotrile inhibited cells showed no spontaneous recovery within 20 min to 30 min. Pretreatment with reserpine and alpha-methyl-paratyrosine abolished amphetamine induced inhibition but only slightly attenuated lergotrile induced inhibition. Lergotrile also blocked the apparent activation of striatal DA synthesis caused by total inhibition of DA impulse flow with gamma-hydroxybutyric acid. It is suggested that lergotrile is a rapidly acting DA agonist somewhat similar to apomorphine and that lergotrile interacts with both presynaptic and postsynaptic DA receptors. 1 reference. (Author abstract modified)

001279 Wehry, S. M.; Carr, L. A. University of Louisville, Louisville, KY 40201 **Effect of d-amphetamine on the inhibition of brain catecholamine turnover induced by cycloheximide.** Pharmacologist. 19(2):195, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effect of dextroamphetamine on the inhibition of brain catecholamine turnover induced by cycloheximide and the differences in the response of various mouse strains to the amnesic effects of cycloheximide and in dextroamphetamine induced reversal of the memory disrupting effects of cycloheximide was reported. The synthesis and metabolism of brain norepinephrine (NE) and dopamine (DA) were determined following the intravenous injection of radiolabeled tyrosine. One hour after administra-

tion of cycloheximide, NE synthesis was significantly decreased in both DBA/2J mice and C57B1/6 mice whereas DA synthesis was decreased only in the C57B1/6 strain. When dextroamphetamine was administered to mice pretreated with cycloheximide, there was a marked increase in the concentration of normetanephrine only in the C57B1/6 strain. Treatment with both drugs appeared to attenuate the inhibition of catecholamine synthesis in the C57B1/6 strain whereas there was a greater decrease in synthesis in the DBA/2J strain. The results support the hypothesis that the amnesic actions of cycloheximide may be due in part to inhibition of catecholamine synthesis and that dextroamphetamine may reverse these effects in the C57B1/6 strain by increasing the release of NE. (Author abstract modified)

001280 Weibel, S. L.; Wolf, H. H. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Stereoselective, dose-dependent modification of intracranial self-stimulation (ICSS) by centrally administered levorphanol and dextrorphan.** Pharmacologist. 19(2):141, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the mechanism by which narcotic drugs affect intracranial self-stimulation (ICSS) in rats was reported. The narcotic drug levorphanol (LEV) enhanced the response rates for ICSS after intraventricular administration of low doses; higher doses of LEV decreased responding. Intraventricular administration of dextrorphan, the nonnarcotic stereoisomer of LEV, produced minimal changes in response as compared to controls. It is suggested that the results support the hypothesis that narcotics increase ICSS at low doses and decrease ICSS at moderate doses by acting stereoselectively at central opiate receptors. (Author abstract modified)

001281 Weiner, William J.; Goetz, Christopher; Nausieda, Paul A.; Klawans, Harold L. Department of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, 1753 West Congress Parkway, Chicago, IL 60612 **Clonazepam and 5-hydroxytryptophan-induced myoclonic stereotypy.** European Journal of Pharmacology (Amsterdam). 46(1):21-24, 1977.

To examine the relation of clonazepam to the central serotonin system, clonazepam was administered to young guinea-pigs, and its effects on 5-hydroxytryptophan (5-HTP) induced myoclonic stereotypy and on whole brain serotonin were assessed. While clonazepam induces a moderate elevation of whole brain serotonin, the drug fails to potentiate or inhibit 5-hydroxytryptophan induced stereotypy in young guinea-pigs. These results suggest that despite drug induced alterations in serotonin concentration clonazepam does not have an effect on the physiologic activity of serotonin and may not exert its pharmacologic activity by influencing serotonin within the brain. 9 references. (Author abstract modified)

001282 Wichert, P. von; Schmidt, C.; Pomranke, K.; Wiegers, U. 1. Medizinische Klinik, Universitats-Krankenhaus Eppendorf, Martinistr. 52, D-2000 Hamburg 20, Germany **Incorporation of radioactive labelled cholin and palmitate into lung lecithin of rabbits treated with high doses of bromcarbamides, barbiturates and diazepam.** Archives of Toxicology (Berlin). 37(2):117-122, 1977.

Because bromcarbamides, often used as mild hypnotics with almost no side-effects at therapeutic dosages, have recently found increasing use in suicidal attempts, a study was made of their pathological mechanism. It has been shown that lungs of patients with bromcarbamide intoxication resemble so called shock lung, and thus incorporation of radioactive labeled choline and palmitate into lung lecithin was measured in rabbits treated with high doses of bromcarbamides and compared with effects of barbiturates and diazepam, which also are often used as suicide drugs. The amount of drugs used was well above the LD50 and was related to the amounts producing severe intoxications in man, often followed by serious pulmonary and respiratory problems. The lower incorporation of palmitic acid compared with normal or increased incorporation of choline as a marker for lecithin synthesis obtained suggests enhanced synthesis of other lecithins that may have lower surface properties. Surfactant metabolism is more markedly altered in bromcarbamide intoxication than in the barbiturate or diazepam group. This is consistent with the clinical observation that mainly bromcarbamides lead to severe respiratory problems. 22 references.

001283 Wielosz, Marian; Dall'olio, Alberto; De Gaetano, Giovanni; Garattini, Silvio. Dept. of Pharmacology, Institute of Clinical Pathology, Medical School, Lublin, Poland **Effect of two non tricyclic antidepressant drugs on (14C)5-hydroxytryptamine uptake by rat platelets.** Journal of Pharmacy and Pharmacology (London). 29(9):546-549, 1977.

The in vitro effects of 3-(p-trifluoromethylphenoxy)-N-methyl-3-phenylpropylamine (Lilly-110140) and of trazodone on the kinetics of radiolabeled serotonin (5-hydroxytryptamine, 5-HT) uptake by rat platelets were investigated to characterize their mechanism of action. A potential metabolite of trazodone, m-chlorophenylpiperazine (CPP) was also investigated. Lilly-110140 was as active as chlorimipramine and several times more active than imipramine as an inhibitor of 5-HT uptake. Like chlorimipramine, Lilly-110140 appeared to be either a noncompetitive inhibitor or an uncompetitive inhibitor of 5-HT uptake, depending upon the concentration of drug used. Trazodone also inhibited 5-HT uptake by platelets, but to a lesser extent than chlorimipramine, imipramine, or Lilly-110140. CPP was about 3 times more potent an inhibitor than was the parent molecule. Both compounds acted noncompetitively. The results are compared with published data on the actions of these compounds on brain 5-HT, and it is posited that rat platelets are a useful pharmacological model of serotonergic nerve endings. 14 references. (Author abstract modified)

001284 Wiesel, Frits-Axel. Division of Neuropsychopharmacology, Dept. of Pharmacology, Karolinska Institutet, S-10401 Stockholm, Sweden **Effects of the isomeric forms of propranolol on central monoamine metabolism in regions of rat brain.** Progress in Neuro-Psychopharmacology (Oxford). 1(1/2):83-89, 1977.

To ascertain whether the effect of d,l-propranolol on central monoamine metabolism may be due to a beta-receptor blockade (l-propranolol) or membrane stabilization (d-propranolol), rats were treated with the isomeric forms of propranolol. Levels of the monoamine metabolites 3-methoxy-4-hydroxyphenylglycol (MOPEG), homovanillic acid (HVA) and 5-hydroxyindole-3-acetic acid (5-HIAA) were determined by mass fragmentography in regions of rat brain. After d,l; and l-propranolol the MOPEG content in brain increased significantly. The HVA level was preferentially increased in a limbic brain region, the olfactory turbercle. The 5-HIAA content was diminished or unchanged irrespective of the isomeric forms of propranolol. It is suggested that the elevated levels of MOPEG and HVA after l-propranolol may be of relevance for the antipsychotic properties suggested for d,l-propranolol. 24 references. (Author abstract modified)

001285 Wilcox, George L. University of Minnesota, Minneapolis, MN 55455 **Effects of antinociceptive drugs on the dorsal root potential in the rat.** Pharmacologist. 19(2):171, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of antinociceptive drugs on the long negative wave of the dorsal root potential (DRP), an indicator of presynaptic inhibition at the first sensory synapse in the CNS, was reported. The actions of the drugs on DRPs evoked by suprathreshold electrical stimulation of the hindpaw in the anesthetized rat were examined. Morphine and oxotremorine, both of which exhibit antinociceptive activity at both segmental and supraspinal levels of the CNS, were administered directly to the spinal cord by push/pull cannulae and intravenously. Morphine reduced the overall amplitude of the DRP; this effect was reversed by naloxone. Oxotremorine reduced only the earliest inhibitory component of the DRP; this effect was reversed by atropine. It is suggested that decreased DRP amplitude may indicate increased tonic levels of inhibition. It is also suggested that since narcotic and muscarinic agonists have different effects on the DRP, they may act via different synaptic mechanisms in the spinal cord. (Author abstract modified)

001286 Williams, Norman; Clouet, Doris H.; Misra, Anand L.; Mule, Salvatore. New York State Offc. of Drug Abuse Services Testing and Research Lab., 80 Hanson Place, Brooklyn, NY 11217 **Cocaine and metabolites: relationship between pharmacological activity and inhibitory action on dopamine uptake into striatal synaptosomes.** Progress in Neuro-Psychopharmacology. 1(3/4):265-269, 1977.

The activity of some cocaine metabolites (norcocaine, benzoylnorecgonine, and ecgonine) and of a stereoisomer of cocaine, pseudococaine, was examined on the high affinity uptake of dopamine into isolated striatal synaptosomes of rat brain. High affinity uptake of dopamine into synaptosomal fractions isolated by gradient centrifugation from rat striatum was inhibited competitively by norcocaine and pseudococaine, as well as by cocaine, with KI50s of 8x10-5 M, 5x10-4 M, and 7x10-6 M, respectively. Benzoylnorecgonine and ecgonine methylester inhibited dopamine uptake about 50% at 5x10-3 or higher. Benzolynorecgonine and ecgonine showed no inhibition at these concentrations but the benzoyl derivatives inhibited dopamine uptake slightly at concentrations of 10-7 or lower. It is noted that striatal dopaminergic nerve endings are similar to noradrenergic neurons of whole rat brain in their lack of discrimination between cocaine and norcocaine. 11 references. (Author abstract modified)

001287 Wilson, Catherine A.; Andrews, M.; Hadley, J. C.; Lemon, M.; Yeo, T. Royal Veterinary College, Royal College Street, London NW1 OTU, England **The role of hypothalamic serotonin (5HT) before ovulation in immature rats treated with pregnant mare serum (PMS).** Psychoneuroendocrinology (Oxford). 2(3):267-274, 1977.

The role of hypothalamic serotonin (5HT) before ovulation in immature rats treated with pregnant mare serum (PMS) is studied. It is noted that p-chlorophenyl-alanine reduces 5HT metabolism in the hypothalamus within two hours of administration and its antiovulatory effect can be overcome by 5HT. This indicates that hypothalamic 5HT activity is essential for the gonadotrophin surge. It is concluded that 5HT has a biphasic effect on gonadotrophin release; it inhibits release if levels are raised on the day of the preovulatory surge, but is essential for release on the day before the expected gonadotropin surge. 18 references. (Author abstract modified)

001288 Wolfe, Gary W.; Bousquet, William F.; Schnell, R. Craig. Dept. of Pharmacology and Toxicology, School of Pharmacy and Pharmaceutical Sciences, Purdue University, West Lafayette, IN 47907 **Circadian variations in responses to amphetamine and chlorpromazine in the rat.** Communications in Psychopharmacology. 1(1):29-37, 1977.

Circadian variations in response to d-amphetamine and chlorpromazine were investigated in rats. A time dependent alteration in d-amphetamine induced locomotor activity was exhibited with peaks of response occurring at 1600 hr and 0400 hr and nadirs at 1200 hr and 2000 hr. The in vivo disposition (brain and plasma) of d-amphetamine measured at the times of peak and nadir locomotor activity response did not differ. Following administration of chlorpromazine (CPZ), a circadian variation in the drug induced hypothermia was exhibited with the greatest decrease in body temperature occurring at 1200 hr. Measurements of in vivo disposition (brain and plasma) of CPZ did not vary at different times of the day. These data suggest that the temporal variations observed in response to d-amphetamine and CPZ do not result from alterations in drug disposition but may reflect time dependent changes in tissue sensitivity to these CNS agents. 10 references. (Author abstract)

001289 Woo, G. K.; Kolis, S. J.; Schwartz, M. A. Hoffman La-Roche Inc., Nutley, NJ 07110 **In vitro metabolism of an imidazobenzodiazepine.** Pharmacologist. 19(2):164, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the in vitro metabolism of 8-chloro-6(2-fluorophenyl)-1-methyl-4H-imidazo-(1,5-a)(1,4)benzodiazep ne maleate (I) was reported. The parent imidazobenzodiazepine was incubated with rat liver supernate fortified with an NADPH generating system. Metabolite II and metabolite III were formed by hydroxylation at the C-1 and C-4 positions, respectively. Metabolite IV was formed by hydroxylation at each of these positions. Phenobarbital pretreatment of rats stimulated the metabolism of the parent compound in vitro. The structures of the parent substance and the three metabolites are illustrated. (Author abstract modified)

001290 Yehuda, Shlomo; Frommer, Reuven. Psychopharmacology Lab., Dept. of Psychology, Bar-Ilan University, Ramat-Gan, Israel **The thermal effects of interaction between d-amphetamine and antidepressants among rats kept at various ambient temperatures.** Communications in Psychopharmacology. 1(6):581-588, 1977.

The thermal effects of interaction between d-amphetamine and three antidepressants, desipramine, clomipramine and maprotiline, on rats kept at 4 and 20 degrees C were studied, noting that modification of the d-amphetamine hypothermia by any of the drugs would suggest that it interacts with central dopaminergic receptors. Results indicate a clear rank order of potency of central dopaminergic activation among the three antidepressants; desipramine was most potent, clomipramine the second most active, and maprotiline had no effect. Other findings are presented to indicate the central dopaminergic action of desipramine and clomipramine. 21 references. (Author abstract modified)

001291 Yeung, Joseph C.; Yaksh, Tony L.; Rudy, Thomas A. School of Pharmacy, University of Wisconsin, Madison, WI 53706 **Concurrent mapping of brain sites for sensitivity to the direct application of morphine and focal electrical stimulation in the production of antinociception in the rat.** Pain (Amsterdam). 4(1):23-40, 1977.

The effect of morphine microinjection and focal electrical stimulation on rats' response to radiant heat and noxious pinch was studied concurrently at 117 brain loci extending from the medial thalamus caudally to the periaqueductal gray area (PAG). Three populations of brain sites were discernible based on their responsiveness to focal electrical stimulation and morphine microinjection in the production of antinociception: 1) sites which support stimulation produced analgesia (SPA, n=24); 2) sites which were sensitive to the direct application of morphine (n=8); 3) sites responsive to both manipulations (n=8). With few exceptions, all morphine sensitive sites were located within the anatomical boundaries of the PAG while sites supporting SPA were located not only within the PAG but also in the brain regions peripheral to this structure. Sites responsive to both manipulations were generally distributed throughout the lateral aspect of the posteroventral PAG. Stimulation strength/effect curves for sites subserving SPA were also obtained. No differences were discovered between curves obtained from morphine sensitive and insensitive brain loci. 40 references. (Author abstract)

001292 Yih, Tjong Ding; van Rossum, Jacques M. Dept. of Pharmacology, University of Nijmegen, Geert Grooteplein Noord 21, Nijmegen, The Netherlands **Pharmacokinetics of some homologous series of barbiturates in the intact rat and in the isolated perfused rat liver.** Journal of Pharmacology and Experimental Therapeutics. 203(1):184-192, 1977.

The pharmacokinetics of a number of 5,5-dialkyl substituted barbiturates was studied in the intact rat and in isolated perfused rat liver. The rate of elimination for the barbiturates (as measured against a reference compound) was structure dependent and seemed to be correlated with the lipophilicity of the compounds expressed as the octanol/water and hepatocytes/water partition coefficient. Half-life decreased with the introduction of a larger alkyl side-chain and with substitution of a bromoallyl group instead of an allyl group. A more rapid elimination was also induced by the introduction of a methyl group onto the nitrogen of the barbiturate nucleus. The elimination clearance constants relative to the heptabarbital clearance were in the same order of magnitude as those found in humans. It is suggested that the clearance values for barbiturates in humans may be predicted by studying the relative values in rats. 32 references. (Author abstract modified)

001293 Zarzecki, P.; Blake, D. J.; Somjen, G. G. Dept. of Physiology, Queen's University, Kingston K7L 3N6, Canada **Neurological disturbances, nigrostriate synapses, and iontophoretic dopamine and apomorphine after haloperidol.** Experimental Neurology. 57(3):956-970, 1977.

To test the hypothesis that haloperidol blocks the effects of dopamine in the caudate nucleus, nigrostriate synaptic transmission was studied by recording single unit responses and evoked potentials and by microiontophoresis in the caudate nucleus of unanesthetized cats. In acute experiments performed after the development of parkinsonian like motor disorders, neurons responded to stimulation of the substantial nigra and to the microiontophoresis of dopamine in manners and in proportions indistinguishable from those seen in normal cats. Apomorphine inhibited three of nine neurons also inhibited by dopamine. Nigrostriate evoked potentials of normal waveform and amplitude were present. In another group of cats, a single dose did not modify the evoked potentials during the time when biochemical changes are known to be occurring. In conclusion, a change in the effectiveness of dopamine on neurons in the caudate nucleus (including some also influenced by apomorphine) could not be detected after systemic haloperidol. Nigrostriate synaptic transmission (including that to neurons also influenced by dopamine) was not blocked. These findings are not consistent with the theory that the behavioral effects of systemically administered haloperidol are caused by a blockade of dopaminoceptive synapses in the caudate nucleus. 22 refereences. (Author abstract modified)

001294 Ziance, Ronald J. Dept. of Pharmacology, University of Georgia, School of Pharmacy, Athens, GA 30602 **Specificity of amphetamine induced release of norepinephrine and serotonin from rat brain in vitro.** Research Communications in Chemical Pathology and Pharmacology. 18(4):627-644, 1977.

In a study of the specificity of amphetamine induced release of norepinephrine (NE) and 5-hydroxytryptamine (5-HT) from rat brain, incubation of normal rat cortical or brainstem tissue with 3H-NE or 3H-5-HT and subsequent exposure to amphetamine produced a concentration related release of the transmitters from tissue stores into the incubation media. Although pretreatment with the catecholamine neurotox in 6-hydroxydopamine (6-OHDA) reduced the retention of 3H-NE in both of these tissues, the proportion of 3H-NE released by amphetamine was attenuated only in cortical tissue. Pretreatment with the serotonergic neurotoxin, 5,6-dibydroxytryptamine (5,6-DHT) had no effect on the retention or release of 3H-NE in cortical or brainstem tissue. Pretreatment with 5,6-DHT reduced the retention of 3H-5-HT in the cortex and brainstem, but the release of 3H-5-HT, was significantly attenuated only in the latter tissue. 6-OHDA pretreatment increased the retention and proportion of cortical 3H-5-HT released by amphetamine but reduced the release of brainstem 3H-5-HT in the absence of an effect on retention. It appears that the in vitro release of 3H-NE from the cerebral cortex occurs primarily from catecholamine and not serotonergic neurons whereas the cortical release of 3H-5-HT is not an event specific to serotonergic nerve terminals. The release of 3H-5-HT from brainstem does not appear to be restricted to the serotonergic cell bodies since its release was attenuated by 5,6-DHT and 6-OHDA. 33 references. (Author abstract)

04 MECHANISM OF ACTION: BEHAVIORAL

001295 Abdallah, Abdulmuniem H.; Riley, Cathryne C.; Boeckler, Walter H.; White, Judith A. Dow Chemical Company, Midland, MI 48640 **The effect of subchronic administration of lithium carbonate on the pharmacological activity of d-amphetamine.** Pharmacologist. 19(2):227, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of subchronic administration of lithium carbonate on the pharmacological activity of dextroamphetamine in male mice was reported. The ingestion of a diet containing 1% lithium carbonate did not significantly alter the effect of dextroamphetamine on total spontaneous activity. Intraperitoneal administration of lithium carbonate twice a day for 10 da failed to significantly alter the effect of dextroamphetamine on total spontaneous activity. However, the same dose of lithium carbonate for 12 da caused an increase in dextroamphetamine induced circling, gnawing, and licking behavior and a decrease in salivation. The ingestion of lithium carbonate in diet for 47 da had an effect only on dextroamphetamine induced circling. In the open field study, dextroamphetamine caused a significant decrease in the rearing behavior of mice and an increase in their entry into the lighted area. The ingestion of lithium carbonate for 33 da antagonized the effect of dextroamphetamine on mouse entry into the lighted area. (Author abstract modified)

001296 Aceto, Mario D.; Carchman, Richard A.; Harris, Louis S.; Flora, Roger E. Medical College of Virginia, Richmond, VA 23298 **Caffeine elicited withdrawal signs in morphine-dependent rhesus monkeys.** Pharmacologist. 19(2):144, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the interaction between caffeine or sodium benzoate and morphine in monkeys was reported. In morphine dependent monkeys, caffeine produced most of the signs commonly seen after the administration of naloxone. In naive monkeys, caffeine elicited some withdrawal symptoms but the effect was much weaker than that seen in morphine dependent monkeys. Sodium benzoate also elicited some withdrawal signs in morphine dependent monkeys, but had little effect in naive animals. Since it has been reported by other investigators that caffeine is more potent than sodium benzoate in inhibiting cyclic 3',5'-adenosine monophosphate (cAMP) phosphodiesterase activity, the results are suggested to be consistent with the idea that morphine withdrawal in rodents is associated with increased brain levels of cAMP. (Author abstract modified)

001297 Ahlenius, Sven; Engel, Jorgen; Zoller, Madeleine. Department of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg 33, Sweden **Effects of apomorphine and haloperidol on exploratory behavior and latent learning in mice.** Physiological Psychology. 5(3):290-294, 1977.

In order to characterize the behavioral effects produced by drug induced changes in central dopamine neurotransmission, the behavior of mice was studied in a maze. The animals were given haloperidol, apomorphine, or solvent vehicle, during a 30 and 10 min time of preexposure to the maze, respectively, and their exploratory activity was recorded. The ability of these animals to find food in the same maze was later (plus 24 h) compared with the performance of a group not previously exposed to the maze (naive). In comparison with naive animals, untreated mice preexposed to the maze displayed a more efficient performance (latent learning) when trained to find food in the maze. It was found that haloperidol or apomorphine significantly suppressed the exploratory behavior of the animals during the time of preexposure. However, animals thus treated learned the maze 24 h later as rapidly as animals treated with solvent vehicle. Higher doses of apomorphine also produced a suppression of exploratory behavior similar to that seen after its administration at lower doses, or after treatment with haloperidol; however, these animals did not display latent learning 24 hrs later. 11 references. (Author abstract)

001298 Allikmets, L. Kh.; Zharkovskiy, A. M.; Vasar, E. E. Kafedra farmakologii, Tartuskiy universitet, Tartu, USSR **/Antagonism between the effects of l-dopa and apomorphine on the behavior of rats./** Antagonism mezhdu l-dofa i apomorfinom v ikh effektakh na povedeniye krys. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 84(7):51-53, 1977.

Effects of simultaneous injections of apomorphine and l-dopa on stereotypy, aggressiveness, exploratory motor activity, and threshold of emotional reactivity, and aggressiveness elicited by painful electrical stimulation were studied in male albino rats. When injected separately, both compounds had similar effects on exploratory motor activity and emotional behavior, but when injected simultaneously in various doses, a distinct antagonism between l-dopa and apomorphine was noted. When injected with l-dopa, apomorphine increased dopamine content of the forebrain and the diencephalon. It is suggested that an increased level of functionally active mediator supresses the activity of postsynaptic receptors which are sensitive to it. 13 references. (Journal abstract modified)

001299 Altman, Jack L. INRS-Sante, Universite du Quebec, Montreal, Gamelin, Quebec H1N 3M5, Canada **Drugs and the production of temporal intervals in the rat.** Progress in Neuro-Psychopharmacology. 1(3/4):301-308, 1977.

A study is reported investigating the production of temporal intervals by drugs in the rat. In a paradigm similar to human timing procedures, water deprived rats were differentially reinforced for depressing a level for 4.5to 5.5sec. Administration of amphetamine and tetrahydrocannabinol resulted in premature release of the lever ("short" errors); lysergic acid diethylamide and chlorpromazine prolonged depression of the lever beyond the required interval ("long" errors). The procedure employed appears sensitive to drug induced shifts in timing behavior and permits direct comparison between the results of timing experiments with lower animals and the data obtained from the temporal production experiments commonly used with humans. 42 references. (Author abstract modified)

001300 Anden, N.-E.; Strombom, Ulf; Svensson, T. H. Department of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg, Sweden **Locomotor stimulation by L-dopa: relative importance of noradrenaline receptor activation.** Psychopharmacology (Berlin). 54(3):243-248, 1977.

The importance of brain noradrenaline synthesis and receptor activation for the hyperkinesia induced by carbidopa plus L-dopa in reserpine treated or normal mice was analyzed in four different models. After pretreatment with reserpine and the monoamine oxidase inhibitor nialamide, the hyperkinesia induced by L-dopa was partly mediated via stimulation of noradrenaline receptors since it was significantly antagonized by the noradrenaline receptor blocking agent phenoxybenzamine. Treatment with reserpine plus L-dopa produced an increase in motor activity probably due to stimulation of dopamine receptors since it was not accompanied by an accumulation of noradrenaline and it was not inhibited by phenoxybenzamine. The hyperkinesia following treatment with reserpine and a higher dose of L-dopa was probably due to stimulation of both dopamine and noradrenaline receptors since the dopamine-beta-hydroxylase inhibitor FLA-63 partly reduced the effect of L-dopa. Phenoxybenzamine potentiated the motor stimulation by L-dopa in mice not pretreated with reserpine, perhaps depending on a slight enhancement of the net accumulation of brain dopamine. Thus, noradrenaline receptor activation is of importance for the L-dopa induced hyperkinesia, at least after high doses or after monoamine oxidase inhibition. 25 references. (Author abstract)

001301 Antelman, Seymour M.; Black, Cynthia A.; Rowland, Neil E. Psychobiology Program, Dept. of Psychology, University of Pittsburgh, School of Medicine, Pittsburgh, PA 15260 **Clozapine induces hyperphagia in undeprived rats.** Life Sciences (Oxford). 21(12):1747-1749, 1977.

To determine the effects of the neuroleptic clozapine on undeprived rats, male albino rats were injected with clozapine and given 2 hr feeding tests immediately following injection. Both peripheral and central injections of clozapine produced dose dependent increases in food intake compared to vehicle treated animals. No differences in water intake were noted. Results of this and other studies indicate that the antiadrenergic properties of both clozapine and the phenothiazines play a key role in their ability to induce feeding, and bring into question the purely adrenergic theory of feeding. 18 references.

001302 Appel, James B; Joseph, James A.; Utsey, Earl; Hernandez, Linda L.; Boggan, William O. Dept. of Psychology, University of South Carolina, Columbia, SC 29208 **Sensitivity to psychoactive drugs and the serotonergic neuronal system.** Communications in Psychopharmacology. 1(6):541-551, 1977.

The role of serotonin (5-HT) containing neurons in mediating sensitivity to the behaviorally disruptive effects of several psychoactive drugs was assessed in rats which had been trained to lever press on a fixed-ratio schedule of water reinforcement (FR 32). In three pretreatment conditions, animals were given i.v. injections of 5,7-dihydroxytryptamine (5,7-DHT), three daily i.p. injections per week of p-chlorophenylalanine methyl ester (PCPA), or i.p. injections of p-chloroamphetamine (PCA). The following agents were then given in random order beginning 12 days after pretreatment: LSD, quipazine, mescaline, amphetamine, and phencyclidine. Whole brain concentrations of 5-HT and norepinephrine (NE) were determined 1) following pretreatment with 5,7-DHT or PCA and following chronic PCPA administration in separate nontrained groups of animals. The results indicated that 5,7-DHT and PCPA, potentiate the behaviorally disruptive effects of LSD, psilocybin, quipazine and mescaline -- each of which may act (at least in part) as a central 5-HT agonist; none of the pretreatments altered the behavioral effects of phencyclidine or d-amphetamine. It is concluded that the particular pattern of electrophysiological and neurochemical activity induced by pretreatment appears to be a critical determinant of subsequent drug effects. 16 references. (Author abstract modified)

001303 Baldino, F.; Cowan, A.; Geller, E. B.; Adler, M. W. Temple University School of Medicine, Philadelphia, PA 19140 **Effects of antipsychotic and antianxiety drugs on the morphine abstinence syndrome in rats.** Pharmacologist. 19(2):170, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of various doses of chlorpromazine, haloperidol, thioridazine, chlordiazepoxide, and diazepam on the morphine abstinence syndrome in rats was reported. The rats were implanted with morphine pellets for 3 da, after which the drugs being tested were injected subcutaneously 55 min prior to precipitation of abstinence with naloxone. Jumping was exacerbated by chlorpromazine, chlordiazepoxide, and diazepam; haloperidol and thioridazine had no significant effect on this sign. Weight loss over 1 h was decreased only by chlorpromazine and diazepam. Wet dog shakes were decreased by haloperidol, but were increased by chlordiazepoxide and diazepam. Other abstinence signs were not significantly affected. Although each test drug decreases dopamine availability (either directly or indirectly) at the postsynaptic receptor, there is no common influence on individual abstinence signs. It is suggested that the usefulness of the rat model to assess the influence of modifying agents on abstinence signs should be questioned. (Author abstract modified)

001304 Baltzer, John H.; Levitt, Robert A.; Furby, John E. Department of Psychology, Southern Illinois University, Carbondale, IL 62901 **Etorphine and shuttle-box self-stimulation in the rat.** Pharmacology Biochemistry and Behavior. 7(5):413-416, 1977.

To examine the effect of etorphine on shuttlebox self-stimulation and to evaluate the development of tolerance, rats were trained to turn rewarding electrical brain stimulation on and off by crossing back and forth in a shuttlebox. Moderate doses of the narcotic analgesic, etorphine, increased mean ON times while having little effect on OFF times. Tolerance did not develop to the reward enhancement action over 5 consecutive days of injections. This paradigm seems valuable for exploration of the reinforcing properties of narcotic drugs. 21 references. (Author abstract modified)

001305 Barrett, J. E.; Dworkin, S. I.; Zuccarelli, R. R. Dept. of Psychology, University of Maryland, College Park, MD 20742 **Effects of d-amphetamine, chlordiazepoxide and promazine on responding of squirrel monkeys maintained under fixed-interval schedules of food presentation and stimulus-shock termination.** Pharmacology Biochemistry & Behavior. 7(6):529-535, 1977.

The effects of d-amphetamine, chlordiazepoxide and promazine on responding of squirrel monkeys maintained under fixed-interval schedules of food presentation and stimulus shock termination were studied. Under the stimulus shock termination schedule, shocks occurred independently of responding, on the average of every 3 minutes; a response after 5 min terminated the prevailing stimulus and shock-presentation schedule. d-Amphetamine increased and promazine decreased responding under both fixed-interval schedules. Chlordiazepoxide increased responding maintained by food presentation but decreased responding maintained by termination of the stimulus shock complex. Results indicate that under certain conditions and with certain drugs, the event that maintains responding can determine the effects a drug will have on behavior. 24 references. (Author abstract modified)

001306 Barrett, James E. Department of Psychology, University of Maryland, College Park, MD 20742 **Behavioral history as a determinant of the effects of d-amphetamine on punished behavior.** Science. 198(4312):67-69, 1977.

The behavioral effects of d-amphetamine were examined in four male squirrel monkeys for which responding maintained by food was also punished by shock. Two of these monkeys were experimentally naive and two had a history of responding maintained by both shock postponement and shock presentation schedules. In accord with earlier studies, d-amphetamine did not increase punished responding by naive monkeys but did increase punished responding in the others. It was found that d-amphetamine increased punished responding by the initially naive monkeys after they were trained under a shock postponement schedule. It is shown that prior experience can leave residual effects that, although not manifest in current behavior, can nonetheless significantly influence the behavioral effects of drugs. 13 references. (Author abstract modified)

001307 Batty, J.; Meyerson, B. J. Institute of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **Effects of PCPA on marking behaviour in the male Mongolian gerbil (Meriones unguiculatus).** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):41, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the effects of the serotonin synthesis inhibitor PCPA on an androgen dependent behavior, the scent marking response, was studied in castrated male Mongolian gerbils injected with testosterone propionate to maintain marking at approximately 40% of presaturation levels. PCPA treated animals showed significantly more marking responses than control, with no changes in ambulation. The results suggest that serotonergic mechanisms are involved in the control of this behavior.

001308 Beaton, John M.; Liu, Wu-Fuu; Teague, Robert S. Neurosciences Program, University of Alabama in Birmingham, Birmingham, AL 35294 **The effects of psychotomimetic drugs on the conditioned emotional response.** Pharmacologist. 19(2):174, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of N,N-dimethyltryptamine (DMT), dextroamphetamine, and mescaline on rat operant behavior before and after the superimposition of a conditioned emotional response (CER) via shock stress was reported. Rats were trained on a variable interval 30 sec schedule of reinforcement. After initial testing of each dosage of each drug in all animals, the CER schedule was superimposed. The drugs were tested again at each dose level after the CER was well established. Comparison of the data for the rate of bar-pressing and number of reinforcements obtained for the pre-CER and post-CER conditions revealed that the addition of shock stress via the CER schedule potentiated the behavior disruptive effects of 1mg/kg dextroamphetamine, 10mg/kg mescaline, and 5mg/kg/DMT. (Author abstract modified)

001309 Beckwith, Bill E.; O'Quin, R. Karen; Petro, Marilyn S.; Kastin, Abba J.; Sandman, Curt A. Ohio State University, Columbus, OH 43210 **The effects of neonatal injections of alpha-MSH on the open-field behavior of juvenile and adult rats.** Physiological Psychology. 5(3):295-299, 1977.

Male and female infant albino rats, between the ages of 2 and 7 days, were treated with either Melanocyte Stimulating Hormone (MSH) or the vehicle solution and then tested in an open-field apparatus when they were 45 days old and again when they were 120 days old. Treatment with alpha-MSH resulted in greater body contact of adult males both at 45 and at 120 days of age. Females treated with alpha-MSH exhibited greater body contact when tested at 45 days of age, but did not display increased body contact when tested at 120 days of age. These results are indicative of a sex difference in response to neonatal administration of alpha-MSH. 31 references. (Author abstract)

001310 Bedard, P.; Pycock, C. J. Laboratoires de Neurobiologie, Pavillon Notre-Dame, 2075 rue de Vitre, Quebec G1J 5B3, Canada **'Wet-dog' snake behaviour in the rat: a possible quantitative model of central 5-hydroxytryptamine activity.** Neuropharmacology (Oxford). 16(10):663-670, 1977.

The wet dog shake (WDS) response was investigated in the rat as a possible animal model to quantify central 5-hydroxytryptamine (5-HT) activity. The behavior occurs in a dose dependent manner following systemic administration of the 5-HT precursor, 5-hydroxytryptophan (5-HTP). It is also seen after injection of L-tryptophan and the proposed 5-HT agonists 5-methoxy-N, N-dimethyltryptamine, lysergic acid diethylamide, and quipazine. Potential 5-HT uptake blocking compounds (chlorimipramine, ORG-6582, femoxetine) only weakly and intermittently induced the phenomenon. The putative 5-HT antagonists, methysergide and cyproheptadine, were effective at blocking 5-HTP induced WDS. Concomitant dopamine receptor stimulation with amphetamine and apomorphine also markedly decreased the 5-HTP induced WDS response. However manipulation of central cholinergic and noradrenergic mechanisms was without effect on 5-HTP induced WDS behavior. It is proposed that the WDS response in rats may provide a quantitative model of central 5-HT activity. It is possibly related to head twitches and jerks described in other animal species. 36 references. (Author abstract modified)

001311 Bedford, J. A.; Lovell, D. K.; Wilson, M. C. Research Institute of Pharmaceutical Science, School of Pharmacy, University of Mississippi, University, MS 38677 **The sociopharmacology of fenfluramine (FM), methylphenidate (MP), and diethylpropion (DP) in Macaque arctoides.** Pharmacologist. 19(2):227, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of fenfluramine, methylphenidate, and diethylpropion on social behavior in a heterosexual group of monkeys (Macaque arctoides) was reported. The effects of methylphenidate and diethylpropion closely resembled those previously reported with dextroamphetamine; e.g.,decreased food consumption, decreased self-grooming, and increased heterosexual presenting. Fenfluramine likewise induced anorexia and increased presenting, but the presenting was homosexual rather than heterosexual. Masturbation was also prominent in the males. The effects of fenfluramine, therefore, did not mimic those of the psychomotor stimulants. Certain aspects of the data indicated that the drug effects may be dependent on the animal's social position. 1 reference. (Author abstract modified)

001312 Blundell, John E.; Strupp, Barbara J.; Latham, Colin J. University of Leeds, Leeds LS2 9JT, England **Pharmacological manipulation of hoarding: further analysis of amphetamine isomers and pimozide.** Physiological Psychology. 5(4):462-468, 1977.

Dose response relationships were established for the effect of d-amphetamine and l-amphetamine on hoarding latency, the time course of hoarding, and the size of the total hoard. Both isomers displayed a marked effect on hoarding latency with the d-isomer approximately twice as potent as the l-form. The effects of the isomers on latency were reflected in the temporal profiles and in the sizes of the accumulated hoards. In a further experiment, pimozide, a dopamine blocking agent, drastically reduced the overall level of hoarding but had only a minor effect on hoarding latency. Pimozide exerted selective action on the amphetamine isomers, markedly antagonizing the effect of d-amphetamine on latency but displaying little effect on the l-form. The results indicate that pharmacological manipulation can reduce hoarding activity in the rat by means of a number of distinct mechanisms. 30 references. (Author abstract)

001313 Bozarth, Michael A.; Reid, Larry D. Rensselaer Polytechnic Institute, Troy, NY 12181 **Addictive agents and intracranial stimulation (ICS): naloxone blocks morphine's acceleration of pressing for ICS.** Bulletin of the Psychonomic Society. 10(6):478-480, 1977.

The effect of a small dose of naloxone on morphine induced acceleration of pressing for intracranial stimulation (ICS) was tested. Subsequent to obtaining stable press rates for each intensity of ICS, five rats received daily injections of morphine (10mg/kg) 4 h prior to testing and five rats were injected with saline. After a significant acceleration of pressing for ICS was demonstrated by the morphine group, both groups were injected with naloxone (1mg/kg) 15 min prior to testing. No effect was shown for the placebo group, while naloxone blocked morphine's potentiation of pressing for ICS. The blocking effect persisted for 3 days after the single dose of naloxone despite the continued administration of morphine (10mg/kg/day), which had previously accelerated pressing for ICS. Results support the conclusion that morphine's acceleration of pressing is the consequence of a specific pharmacological process and not due to a rebound from a depression in ac-

tivity, which would be enhanced by naloxone, or due to general, nonspecific effects of behavior. 11 references. (Author abstract modified)

001314 Bradl, M.; Reim, G. Physiological Institute of the Friedrich-Schiller-University, Teichgraben 8, DDR-69 Jena, Germany **The influence of electrical stimulation on the hippocampal unit's activity of the rabbit.** Activitas Nervosa Superior (Praha). 19(2):113-114, 1977.

A paper delivered at the Second International CIANS Congress (Prague), concerned with the recording of spike trains from hippocampal CA1 units and the occipital EEG in rabbits, is presented. Electrical spontaneous activity and recordings related to generalized afterdischarges were recorded in rabbits awakening from halothane narcosis and rabbits narcotized by urethane and phenobarbitone respectively. Spontaneous EEG showed higher frequency in awake rabbits, with slower waves in urethane and phenobarbitone rabbits. Afterdischarges were detected in awake and phenobarbitone rabbits, while urethane raised the threshold. In all animals, hippocampal spiking was drastically enhanced during afterdischarges in relation to spontaneous spike trains, when hippocampal firing was slower following afterdischarge, perhaps traceable to reverberating mechanisms in the limbic system or confusion of integrative process of hippocampal pyramidal cells. It is suggested that the study of hippocampal spike trains relative to afterdischarges is a step toward the elucidation of the somatic background of the psychoses. 6 references.

001315 Branchey, Marc H.; Cavazos, Lazaro A.; Cooper, Thomas B. Rockland Research Institute, Orangeburg, NY 10962 **Effects of lithium on seizure susceptibility in alcoholized and non-alcoholized rats.** Communications in Psychopharmacology. 1(3):213-224, 1977.

The response to electroshock was compared in 4 groups of rats after 13 weeks of administration of either a control diet (0.95cal/cc), a diet containing lithium (0.8mmol of LiCl/l), a diet containing alcohol (35% of its caloric content) or a diet containing lithium and alcohol. Testing was done at the time of alcohol withdrawal. The sensitivity to electroshock was significantly increased by lithium but not significantly modified by alcohol withdrawal. Discrepancies between the present results and previous ones are noted, possibly traceable to the questionable reliability of audiogenic seizures as an index of alcohol dependence, and differences in the alcohol metabolism of various strains of rats or differences in the accompanying diet. 18 references. (Journal abstract modified)

001316 Brien, J. F.; Peachey, J. E.; Rogers, B. J.; Kitney, J. C. Department of Pharmacology, Faculty of Medicine, Queen's University, Kingston, Ontario K7L 3N6, Canada **Amphetamine-induced stereotyped behaviour and brain concentrations of amphetamine and its hydroxylated metabolites in mice.** Journal of Pharmacy and Pharmacology (London). 29(1):49-50, 1977.

The possible correlation between amphetamine induced stereotypy and brain levels of amphetamine, p-hydroxyamphetamine, and p-hydroxynorephedrine was studied in male Swiss albino mice. (+)-Amphetamine was given i.p. b.i.d. at a 6 hr interval. Mice were rated over a 2 min period for gnawing/licking/sniffing behavior or self-mutilating behavior at 30 min after amphetamine administration. No detectable amounts of p-hydroxyamphetamine or p-hydroxynorephedrine were found in the brains of mice up to 90 min after amphetamine administration to untreated and chronically treated animals. All mice engaged in gnawing/licking/sniffing behavior initially, but some animals switched to self-mutilation during the course of chronic amphetamine treatment. Mice showing gnawing/licking/sniffing behavior had brain amphetamine concentrations of 7.6to 11.8mcg/g, while mice exhibiting self-mutilation had brain amphetamine concentrations of 9.4to 14.0mcg/g. Brain amphetamine concentrations were similar for mice receiving single or multiple drug administrations. 14 references.

001317 Burov, Yu. V.; Kampov-Polevoy, A. B.; Salimov, R. M. Laboratoriya farmakoterpaii ekstremal'nykh sostoyanii, Institut farmakologii AMN SSSR, Moscow, USSR /**Influence of pharmacological agents on avoidance reflexes in a group experiment on rats.**/ Vliyanyie farmakologicheskikh veshchestv na refleks izbeganiya v gruppovom eksperimente krys. Zhurnal Vysshey Nervnoy Deyatel'nosti (Moskva). 27(3):530-533, 1977.

The influence of certain pharmacological agents on avoidance reflexes in rats was studied. Avoidance reflexes were shown to be disturbed when performed in the presence of a group of unconditioned rats. The degree of the disturbance depended on the number of unconditioned animals present and the extent of emotional excitation. Tranquilizers and antidepressants, while improving the avoidance reflex in the presence of a group of excited rats, did not affect the disturbance of avoidance in the presence of a group of calm rats. It is assumed that these drugs prevent the appearance of emotional excitation in learned animals but have no effect on avoidance reflexes in the group of calm rats. 6 references. (Journal abstract modified)

001318 Burov, Yu. V.; Salimov, R. M. Laboratoriya farmakoterapii ekstremal'nykh sostoyaniy, Institut farmakologii AMN SSSR, Moscow, USSR /**Influence of neurotropic drugs on changes of evoked potentials amplitudes after stimulation of the hypothalamus.**/ Vliyaniye neyrotropnykh veshchestv na izmeneniye amplitud vyzvannykh potentsialov posle stimulyatsii gipotalamusa. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova (Moskva). 27(1):186-193, 1977.

Effects of neurotropic drugs on attention span after emotional excitation and changes in the inhibitory processes were studied in unrestrained cats. Records of evoked responses to audible clicks in the cortex, reticular formation and hippocampus, as well as determination of thresholds of hypothalamic stimulation eliciting fear and rage reactions have shown that after emotional excitation hypothalamic excitability is enhanced and the thresholds of perception of foreign signals are higher, causing slackening of attention. Trifluoperazine, haloperidol, diazepam, benactizine, chlordiazepoxide, amitriptyline, and imipramine normalize attention after emotional excitation by reducing excitability of the hypothalamus. Pentobarbital, chlorpromazine, trifluoperazine, and haloperidol accentuate the attention disturbance after emotional excitation due to blockade of the inhibitory action of the basolateral amygdala and dorsal hippocampus on the hypothalamus. 16 references. (Journal abstract modified)

001319 Cannon, H. Eleanor; Staub, Richard A.; Wyatt, Richard Jed; Gillin, J. Christian. Laboratory of Clinical Psychopharmacology, Division of Special Mental Health Research, IRP, Saint Elizabeths Hospital, Washington, DC **Paramethoxyphenylethylamine (PMPEA): some behavioral observations in rats.** Communications in Psychopharmacology. 1(1):71-79, 1977.

The behavioral effects of paramethoxphenylethylamine (PMPEA), the O-methylated derivative of tyramine which is structurally related to mescaline, were studied in rats, and the

interactions between PMPEA and some other compounds were examined. PMPEA appears to be a behaviorally active substance which produces types of behavior similar to those seen in mentally ill individuals. In rats, PMPEA produced a set of behaviors which were dose related. Neither behavioral tolerance to an intermediate dose, nor a behavioral response to a subthreshold does were observed within the limited pradigm of the experiments. Chlorpromazine pretreatment (1.5mg/kg) did not significantly alter rats' response to PMPEA. Pimozide pretreatment of 1.0mg/kg significantly reduced or blocked response to PMPEA. 9 references. (Author abstract modified)

001320 Carlini, E. A.; Lindsey, C. J.; Tufik, S. Departmento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu, 862-1 andar, 04023 Sao Paulo, Brazil **Cannabis, catecholamines, rapid eye movement sleep and aggressive behaviour.** British Journal of Pharmacology (London). 61(3):371-379, 1977

To further elucidate the relationships of cannabis, catecholamines, rapid eye movement (REM) sleep, and aggressive behavior, a series of behavioral and physiological studies were undertaken in REM deprived/nondeprived rats following the administration of dopaminergic drugs and delta9-tetrahydrocannabinol (THC). Previous REM sleep deprivation enhanced both THC induced hypothermia and nomifensine effects on aggressive behavior. A marihuana extract decreased brain dopamine turnover in REM sleep deprived rats, an effect not observed in nondeprived rats. Noradrenaline metabolism was not altered. Fighting behavior was elicited in REM sleep deprived rats treated with 4 different dopamine beta-hydroxylase inhibitors. Apomorphine, nomifensine and THC administered to nondeprived rats pretreated with bis(4-methyl-1-homopiperanzinyl-thiocarbonyl) disulphide (Fla-63), induced fighting behavior. Nomifensine and apomorphine induced fighting in nondeprived rats pretreated with THC. Clonidine inhibited the fighting elicited in REM sleep deprived rats by either THC or Fla-63 pretreatment. The data are discussed in terms of the influence of REM sleep deprivation (or the stress associated with deprivation) on the response to dopaminergic drugs and cannabis. Taken together they emphasize the participation of brain dopamine and noradrenaline systems in the aggressive behavior studied. 38 references. (Author abstract modified)

001321 Carlsson, S. G.; Ahlenius, S. Dept. of Psychology, Univ. of Goteborg, S-40020 Goteborg, Sweden **The effect of amphetamine and L-dopa on tetrabenazine-induced suppression of intracranial self-stimulation in the rat.** Scandinavian Journal of Psychology (Stockholm). 18(2):157-160, 1977.

The effects of amphetamine and L-dopa on tetrabenazine (TBZ) induced suppression of intracranial self-stimulation (ICSS) in rats were examined. A dose dependent increase in the rate of ICSS was seen after L-dopa in animals pretreated with TBZ. d-Amphetamine is believed to act by facilitating the nerve impulse induced release of central catecholamines (CA) whereas the blockage of the granula uptake storage mechanism by TBZ will prevent the storage of CA formed from the administrated L-dopa and thereby interfere with their release by nerve impulses. In the latter case, an activation of central CA receptors in all probability will be due to a dose dependent diffusion of CA from nerve terminals. It is suggested that the failure to completely antagonize the TBZ induced suppression of behavior by L-dopa is due to direct activation, independent of the nerve impulse flow, of central CA receptors easily results in an overstimulation and a reduced specificity in behavior. 17 references. (Author abstract modified)

001322 Carnathan, Gilbert; Meyer, Roger E.; Cochin, Joseph. Alcohol and Drug Abuse Research Center, McLean Hospital, 115 Mill St., Belmont, MA 02178 **Narcotic blockade, length of addiction, and persistence of intravenous morphine self-administration in rats.** Psychopharmacology (Berlin). 54(1):67-71, 1977.

To determine the effects of various levels of naloxone pretreatment on relapse of morphine self-administration, four groups of rats differing in the number of periods of prior exposure to morphine sulphate in the i.v. self-administration paradigm were studied under conditions of narcotic blockade. Three groups of subjects also differing in the amount of prior exposure to morphine sulphate were studied under saline conditions. At effective blocking doses of naloxone, opioid seeking behavior was eliminated in relatively drug naive animals, whereas the persistence of secondary reinforcers in rats with longer addiction histories served to maintain opioid consumption in the presence of adequate pharmacological blockade. Data from saline treated animals were similar to data obtained in naloxone treated animals. It is concluded that at adequate blocking doses of narcotic antagonist, the length of addiction appears to be the best predictor of opioid consumption. 11 references. (Author abstract modified)

001323 Carney, John M.; Rosecrans, John A. Department of Pharmacology, University of Oklahoma School of Medicine, Oklahoma City, OK 73190 **A comparison of the effects of intraventricular morphine and two enzyme resistant enkephalins on operant behavior in the rat.** Pharmacologist. 19(2):189, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of intraventricular administration of morphine and of two enzyme resistant enkephalin analogs on operant behavior in the rat was reported. Water deprived rats were trained to respond under a fixed-ratio 20 schedule for water reinforcement. Morphine produced a dose related decrease in responding which was antagonized by naloxone pretreatment. The two enkephalin analogs also produced dose dependent decreases in responding. On a molar basis, the two enkephalin analogs were about 5 times less potent than morphine in disrupting operant behavior. The response rate decreasing effects of the enkephalins were also blocked by naloxone. (Author abstract modified)

001324 Cattarelli, M.; Vernet-Maury, E.; Chanel, J. Laboratoire de Physiologie neuro-sensorielle, associe du C.N.R.S., Universite Claude Bernard, F-69621 Villeurbanne, France /**Control of the rat olfactory bulb activity induced by biologically significant odors.**/ Modulation de l'activite du bulbe olfactif en fonction de la signification des odeurs chez le rat. Physiology & Behavior. 19(3):381-387, 1977.

The effects of curare and pentobarbital (Nembutal) on responses of rats to stimulus odors were investigated. The animals were stimulated with odors that have been shown in previous experiments to give a distinct emotional behavior. In curarized rats an odor giving alarm behavior evoked a greater number of inhibitory than excitatory responses: a reassuring or a neutral odor evoked an equal number of inhibitory and excitatory responses. After sectioning the olfactory peduncles, the difference in ratio between excitatory and inhibitory responses for alarming or reassuring odors was no longer present. The results are discussed in terms of a modulation of mitral cell activity by higher nervous centers in relation to the biological significance of the stimulus odors. 27 references. (Author abstract)

001325 Chance, William T.; Rosecrans, John A. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Inhibition of drinking by intrahypothalamic administration of morphine.** Nature. 270(5633):167-168, 1977.

The effects of intrahypothalamic applications of morphine on water consumption were investigated in 2 experiments involving 44 adult male rats. Before any morphine tests, stable drinking patterns were established. Morphine was found to block carbachol elicited drinking while not significantly affecting eating, an effect reversed by pretreatment with naloxone. The data demonstrates a potent inhibitory effect of centrally applied morphine across several paradigms of drinking. This antagonism seems to be due to the narcotic properties of the drug and may reflect antimuscarinic cholinergic activity. It is thought that these tests may lead to a simple behavioral test of central narcotic activity. 21 references.

001326 Chance, William T.; Lints, Carlton E. Medical College of Virginia, Richmond, VA 23298 **Eating following cholinergic stimulation of the hypothalamus.** Physiological Psychology. 5(4):440-444, 1977.

Stimulation of the perifornical hypothalamus of satiated rats with both crystalline carbachol and carbachol solutions that elicited eating and drinking was investigated. The eating response did not appear to be a rebound phenomenon, since it paralleled the elicitation of drinking and was not inhibited by repeated applications of crystalline carbachol. Eating following the injection of various doses (0.5, 1.0, 2.0, and 4.0nanomoles) of carbachol also paralleled drinking, showing appropriate dose response relationships. It is hypothesized that cholinergically elicited eating may involve excitatory interaction with adrenergic systems, with increased nicotinic cholinergic activity stimulating alpha-adrenergic neurons to elicit eating. Alternatively, cholinergic stimulation may be activating adrenergic systems through a direct presynaptic release of norepinephrine or epinephrine. 17 references. (Author abstract)

001327 Chapman, Robert H.; Stern, Judith M.; Libert, Jeffrey A. Rutgers State University, Busch Campus, New Brunswick, NJ 08903 **Lordosis reflex, sexual receptivity, and feeding: estrogen responsivity in male and female rats.** Physiological Psychology. 5(3):373-377, 1977.

Possible sex differences in estrogen responsiveness were tested by administering 10 daily injections of 5mg estradiol benzoate to gonadectomized male and female rats. Although estrogen readily potentiated the manually elicited lordosis reflex in both males and females, neither sex showed high levels of sexual receptivity in the presence of a stud male and sex differences were not significant. Reductions in food intake and body weight during estrogen treatment were at least as great in males as in females. Results were discussed in light of accumulating evidence that the male rat is very responsive to estrogen. 21 references. (Author abstract)

001328 Chiba, S.; Young, G. A.; Moreton, J. E.; Khazan, N. Dept of Pharmacology and Toxicology, University of Maryland School of Pharmacy, Baltimore, MD 21201 **Head-shake distributions during self-maintained dependence on morphine, methadone, and l-alpha-acetylmethadol (LAAM) in the rat.** Psychopharmacology (Berlin). 54(1):105-107, 1977.

To determine the relationship between rat head shaking behavior and dependence on morphine, methadone, and l-alpha-acetylmethadol (LAAM), rats were prepared with chronic cortical and muscle electrodes and i.v. cannulas, made tolerant to and physically dependent on morphine, and trained to lever press for i.v. morphine self-injections to maintain dependence. Methadone or LAAM was then substituted for morphine in some rats. During self-maintained dependence on either morphine or methadone, head shakes appeared and increased in frequency before lever pressing for self-injections. In contrast, there were fewer head shakes during LAAM dependence, which were evenly distributed over the entire duration of the interinjection interval. These findings suggest a relationship between head shake distributions, drug seeking behavior, and the pharmacodynamics of these three narcotics. 10 references. (Author abstract modified)

001329 Cole, Sherwood O. Dept. of Psychology, Rutgers University, Camden, NJ 08102 **Interaction of arena size with different measures of amphetamine effects.** Pharmacology Biochemistry & Behavior. 7(2):181-184, 1977.

The effects of various doses of dextroamphetamine on the feeding behavior and activity of rats were investigated in three different size test arenas. Differences in the size of the test arenas significantly altered the drug's effects on ambulatory activity, but not on feeding or rearing. Differences in the size of the arenas significantly altered the interrelationship (correlation) between changes in ambulatory activity and feeding produced by dextroamphetamine, but did not alter the interrelationship between the drug's effects on feeding and rearing. It is suggested that test arena size differentially influences specific measures of amphetamine's effects as well as differentially affecting the correlations of the drug effects. The importance of the interrelationship (correlation) data to the potential incompatibility of the drug's effects is briefly discussed. 5 references. (Author abstract)

001330 Colelli, B.; Sparber, S. B. Department of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **Differential effect of naloxone on fixed ratio operant behavior in stressed and non-stressed rats.** Pharmacologist. 19(2):139, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of naloxone (vs saline control) on fixed ratio (FR) operant behavior in rats subjected to physical stress (via intermittent inescapable footshock) and in nonstressed rats was reported. FR responding by the shocked rats was significantly suppressed compared with the nonshocked rats. Naloxone significantly suppressed responding in the nonshocked animals, but not in shocked rats receiving the same doses. Three months later, the initially nonshocked saline control animals were allowed free access to food prior to behavioral testing, resulting in a suppressed response rate equal to that of the shocked animals receiving saline. Naloxone significantly suppressed responding further, indicating that this differential effect is not rate dependent. It is concluded that some physiological consequence of electrical footshock (perhaps the release of an endogenous opiatelike substance) may be responsible for blocking naloxone's behavioral suppressant effect. (Author abstract modified).

001331 Collaer, Marcia L.; Magnuson, Debra J.; Reid, Larry D. Bradley University, Peoria, IL 61606 **Addictive agents and intracranial stimulation (ICS): pressing for ICS before and after self-administration of sweetened morphine solutions.** Physiological Psychology. 5(4):425-428, 1977.

Press rates for hypothalamic intracranial stimulation (ICS) in rats were measured before and after self-administration of morphine. Rats, fixed with chronically indwelling electrodes for intracranial stimulation (ICS) of the lateral hypothalamic area, pressed a lever for the ICS. They were then given 15

days of opportunity to consume a sweetened morphine solution. They increased their intake of the solution to a mean of 61mg/kg/day of morphine by the 15th day. During the initial days of 37 days of abstinence, they showed pronounced withdrawal symptoms. Subsequently, they were given another opportunity to consume and they relapsed into taking large quantities of morphine. After 10 days of abstinence, rats were tested for pressing for ICS before and after 3 h of opportunity to consume sweetened morphine solution. The rats pressed reliably more after taking the morphine solution than before taking it and more than on days when they only consumed the sweetened solution without morphine. Consequently, it was concluded that pressing for ICS was accelerated after self-administration of morphine by previously addicted rats. 8 references. (Author abstract modified)

001332 Colpaert, F. C.; Niemegeers, C. J. E.; Janssen, P. A. J. Department of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Catecholamine involvement in the narcotic cue.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 226(2):339-340, 1977.

Role of catecholaminergic neurotransmission in the processing of narcotic cue was examined in the rat. Rats were trained to discriminate fentanyl s.c. from saline. Alpha-methyl-p-tyrosine methyl ester i.p. did not affect the discriminability of fentanyl. Rats (n=7) pretreated with either aceperone, dibenamine, propranolol, azaperone, chlorpramazine, pipamperone, pimozide, or spiperone produced attenuated total response output. Phenoxybenzamine pretreatment did not produce attenuated total response. Only pimozide exerted some effect on the narcotic cue and decreased the percentage of responding on selected lever. The latter effect was also observed with spiperone. The data are consistent with the hypothesis that specific neuroleptics (e.g. haloperidol, pimozide) may affect the euphoric action of narcotics in humans. 3 references.

001333 Corson, E. O'L.; Corson, S. A.; Arnold, L. E.; Knopp, W. Lab. of Cerebrovisceral Physiology, Dept. of Psychiatry, College of Medicine, Ohio State University, Columbus, OH 43210 **Long-term elimination of violent behaviour by the interaction of psychopharmacologic and psychosocial therapy.** Activitas Nervosa Superior (Praha). 19(3):216-219, 1977.

In a paper presented at the second international CIANS congress, an overview of the question is there an instinct for aggression or violence is presented, and the interaction of drugs and psychosocial therapy in long-term modification of violent and hyperkinetic behavior is illustrated in a case history of a dog. The dog was uncontrollably violent and exhibited hyperkinesis. After 6 weeks of amphetamine and psychosocial therapy the aggressive behavior largely disappeared and remained modified after the drug was discontinued. It is hypothesized that amphetamine enabled the dog to develop positive adaptive social interaction which seemed to persist even after the drug was discontinued. 11 references.

001334 Costall, Brenda; Naylor, Robert J.; Owen, Richard T. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **Investigations into the nature of the peri-oral movements induced by 2-(N,N-dipropyl)amino-5,6-dihydroxytetralin.** European Journal of Pharmacology (Amsterdam). 45(4):357-367, 1977.

A comparison was made of the doses of neuroleptic and related agents required to inhibit the perioral biting movements induced in the guinea-pig by s.c. administered apomorphine and the s.c. and bilateral intrastriatal injection of 2-(N,N-dipropyl)amino-5,6-dihydroxytetralin. The bilateral intracerebral injection of 2-(N,N-dipropyl)amino-5,6-dihydroxytetralin into areas surrounding the caudate putamen and into the area preoptica and thalamus elicited similar perioral movements but these had a longer latency of onset or shorter duration (anterior, dorsal, and lateral cortex), or were associated with a hyperactivity (area preoptica and thalamus). It is suggested that the mechanisms involved with apomorphine stereotypy differ from those activated by peripherally and intrastriatally administered 2-(N,N-dipropyl)amino-5,6-dihydroxytetralin, and that the preferential detection of oxiperomide and tiapride (clinically effective antidyskinetic drugs), may indicate the usefulness of 2-(N,N-dipropyl)-amino-5,6-dihydroxytetralin as a potential model for predicting antidyskinetic activity. 27 references. (Author abstract modified)

001335 Costall, Brenda; Naylor, Robert J.; Cannon, Joseph G.; Lee, Teresa. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **Differential activation by some 2-aminotetralin derivatives of the receptor mechanisms in the nucleus accumbens of rat which mediate hyperactivity and stereotyped biting.** European Journal of Pharmacology (Amsterdam). 41(3):307-319, 1977.

Behavioral changes induced by a series of dopamine agonists derived from 2-aminotetralin injected directly into the nucleus accumbens were studied in male Sprague-Dawley rats with stereotaxically implanted cannulae. Animals were generally given nialamide i.p. 2 hr before intracerebral injection. A total of 22 2-aminotetralin derivatives was studied. Activity was measured by counting the number of interruptions of a light beam in an activity box during a 5 min period, and stereotyped biting behavior was assessed on a scale of 0 to 4 at intervals of 15 to 30 min. 2-Amino-5,6-dihydroxytetralin and 2-amino-6,7-dihydroxytetralin derivatives were each able to produce hyperactivity and stereotyped behavior, but the former were more potent. The hydroxy groups were essential for activity and dimethoxy derivatives were inactive. Blocking agents for alpha-adrenergic and beta-adrenergic receptors, as well as alpha-methyl-para-tyrosine, failed to reduce the hyperactivity induced by 2-amino-5,6-dihydroxytetralin or the stereotyped behavior induced by 2-(N,N-dipropyl)-amino-5,6-dihydroxytetralin. Both hyperactivity and stereotyped behavior were blocked by haloperidol, indicating that they are dopamine dependent. However, the dopamine mechanisms which regulate hyperactivity and stereotyped behavior in the nucleus accumbens are different. 27 references.

001336 Curry, S. H.; Whelpton, R.; Nicholson, A. N.; Wright, Catherine M. Department of Pharmacology and Therapeutics, London Hospital Medical College, Turner Street, London E1 2AD, England **Behavioural and pharmacokinetic studies in the monkey (Macaca mulatta) with diazepam, nordiazepam and related 1,4-benzodiazepines.** British Journal of Pharmacology (London). 61(3):325-330, 1977.

Behavioral activity (delayed differentiation and spatial delayed alternation) and pharmacokinetics of diazepam and its metabolites, N-desmethyldiazepam (nordiazepam), 3-hydroxydiazepam (temazepam) and 3-hydroxy-N-desmethyldiazepam (oxazepam), and of dipotassium clorazepate (clorazepate), were studied in the monkey (Macaca mulatta). Diazepam and its metabolites and clorazepate were given by intraperitoneal injection. Hydroxylation of diazepam (temazepam and oxazepam) led to a loss of, or a considerable reduction in, behavioral activity, whereas activity was preserved, though

modifed, by demethylation (nordiazepam). It was not possible to establish change in behavior at specific time intervals after clorazepate, but combined performance data revealed an effect. The maximum mean plasma concentrations of diazepam, temazepam, oxazepam and clorazepate were observed at 0.5h, and the maximum mean plasma concentration of nordiazepam was observed at 1 hour. Plasma concentrations of nordiazepam were the highest and decreased monoexponentially. Plasma concentrations of the other drugs declined rapidly at first but more slowly later, and these data were analyzed as biexponential models. In the analysis for metabolites, nordiazepam reached measurable levels after the injection of diazepam and clorazepate. It is suggested that differences in the effects of closely related benzodiazepines may not be due solely to their plasma pharmacokinetic properties, but may arise from differences in their intrinsic activity. 15 references. (Author abstract)

001337 D'Mello, G. D.; Stolerman, I. P. MRC Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Comparison of the discriminative stimulus properties of cocaine and amphetamine in rats.** British Journal of Pharmacology (London). 61(3):415-422, 1977.

To compare the discriminative stimulus properties of cocaine and amphetamine, water deprived rats were trained to press either the left or the right bar in a test chamber according to whether they were injected with a central nervous system stimulant or 0.9% w/v NaCl solution (saline). Correct responses were reinforced with water. Different groups of rats learned to discriminate amphetamine or cocaine from saline. Dose response curves and ED50 values were then determined in brief test sessions when no responses were reinforced. In a crossover study, cocaine was tested in the rats trained to discriminate amphetamine from saline and vice versa. The two drugs were largely interchangeable, but the ED50 values were increased, indicating a possible, subtle difference in their discriminative stimulus properties. The results indicate the importance of complete crossover designs in combination with dose/response determinations when attempting to classify drugs according to their discriminable properties. 23 references. (Author abstract modified)

001338 D'yakova, S. D. Institut vysshey nervnoy deyatel'nosti i neyrofiziologii, Akademiya nauk SSSR, Moscow, USSR **/Dynamics of blood neurotransmitter level as evidence of higher nervous activity changes during chronic administration of seduxen./** Dinamika urovney soderzhaniya neyromediatorov v krovi kak pokazatel' izmeneniy vysshey nervnoy deyatel'nosti pri khronicheskom primenenii seduksena. Zhurnal Vysshei Nervnoy Deyatel'nosti imeni I. P. Pavlova (Moskva). 27(2):382-384, 1977.

Changes of acetylcholine and catecholamine levels in the peripheral blood of dogs were studied during chronic administration of seduxen. It was found that seduxen had excitatory effects on dogs of the passive/defensive type with low initial catecholamine levels, and inhibitory effects on hyperactive/aggressive dogs with high initial levels of catecholamines. These effects were followed by restoration of the acetylcholine/catecholamine equilibrium. Increased seduxen doses had a uniform activating effect, causing absolute increases in catecholamine levels and decreases in acetylcholine levels, expressed in hyperactive and aggressive behavior, rapid pulse and high respiration rate. It is assumed that the paradoxical effects of small seduxen doses result from their influence on nonspecific areas of the limbic/reticular system which reacts according to its functional state and the strength of the stimulant, while the activating effects of large seduxen doses result from excitation of the hypothalamic structures, leading to sympathetic/adrenalin and hypophyseal/hormonal stimulation of the organism. 9 references.

001339 Danielson, T. J.; Wishart, T. B.; Robertson, A.; Boulton, A. A. Psychiatric Research Div., 508A, University Hosp., Saksatoon, Saskatchewan S7N OW8, Canada **Effect of acute and chronic injections of amphetamine on intracranial self-stimulation: amphetamine levels and effects upon some aryl alkyl amines in rat brain.** Progress in Neuro-Psychopharmacology. 1(3/4):279-284, 1977.

The effects of acute and chronic administration of amphetamine on intracranial self-stimulation (ICS) behavior in rats were studied, along with the relationship between ICS and brain amphetamine levels. A biphasic relationship was found between amphetamine and ICS behavior: when brain amphetamine levels were below 1000ng/g ICS behavior was increased, while levels in excess of 100ng/g reduced the rate of responding. Also, prolonged treatment with high doses of amphetamine abolished the rate reducing effect but did not produce enhancement, suggesting that the rate enhancing and rate reducing effects are separate and that tolerance develops to both. Characteristics of the temporal pattern of rate reduction were similar to those produced by drug induced motor deficit. Measurement of cerebral levels of meta-tyramine and para-tyramine showed changes which paralleled the effects of self-stimulation, indicating that changes in the levels of these trace amines can produce changes in the rates of ICS responding and that these rate changes are the result of a motor deficit. 17 references. (Author abstract modified)

001340 Dantzer, R. Station de Pharmacologie-Toxicologie, 180, chemin de Tournefeuille, F-31300 Toulouse, France **Behavioral effects of benzodiazepines: a review.** Biobehavioral Reviews. 1(2):71-86, 1977.

The effects of the benzodiazepines on conditioned and unconditioned behavior in animals are reviewed. These compounds appear to decrease the suppressive effects of aversive stimuli such as electric shock or nonreward on behavior, a result usually related to their anxiolytic activity in human medicine. However, they do not attenuate but rather increase the facilitatory effects of aversive stimuli on behavior. This last result points out the role played by changes at the response level and it is suggested that benzodiazepines induce response perseveration by preferentially interfering with the response produced feedbacks. This effect is further complicated by the role of drug factors and the possibility of the drug treatment to combine to environmental cues and induce state dependency. Further work is needed to examine the interference of benzodiazepine treatment with the facilitatory effects of aversive stimuli on behavior on one hand, and to determine the respective role of exteroceptive cues and response produced feedbacks on the other hand. 192 references. (Author abstract)

001341 Davis, Joel L.; Cherkin, Arthur. VA Hospital, Sepulveda, CA 91343 **Chlorpromazine enhances memory in chicks.** Gerontologist. 17(5, Part II):53, 1977.

In a paper read at the 30th meeting of the Gerontological Society, San Francisco, November 1977, the effect of chlorpromazine (CPZ) on memory was tested on previously trained neonate chicks given either 60 to 144mg CPZ or 15 to 36mg CPZ posttraining. Chicks given higher dosages displayed markedly enhanced 24 hr retention as compared to saline injected controls, while the groups given lower dosage displayed no

memory enhancement. Nonspecific impairment of peck performance was ruled out because CPZ at low or high doses did not reduce pecking in nonaversively trained controls. These results were unexpected and were the reverse of the impairment by CPZ reported in rodents. (Journal abstract modified)

001342 de Lanerolle, Nihal C. Behavioural Physiology Group, Dept. of Animal Science, University of Minnesota, St. Paul, MN 55108 **Amphetamine and chick behaviour: a role for monoamines in the causation of vocalizations and emotions.** Brain, Behavior and Evolution (Basel). 14(6):418-439, 1977.

The effects of amphetamine (AMP) on vocalization and emotional behavior of domestic chicks were studied by methods of direct observation of behavior. Doses of 7.5mg/kg d-amphetamine sulphate injected into 5-day-old chicks characteristically facilitated vocalization - a period of peeps followed by short calls, head shakes, forced locomotion and wing drooping; and decreased the duration of eye closure. AMP also increased the responsiveness of chicks to external stimuli. Bilateral lesions in the midbrain inhibited primarily the vocalizations but not the other behavioral changes produced by AMP. Evidence is presented to explain the neurochemical basis of the AMP induced behavior: namely, that peeping depends on 5-hydroxytryptamine dependent mechanisms, which may also influence the postural changes and head shakes, whereas short calls may be mediated by an interaction between dopaminergic and tryptaminergic mechanisms. It is suggested that the monoamines may also be involved in the attentional changes associated with the vocalizations. 31 references. (Author abstract)

001343 Decsi, L.; Nagy, Julia. Institute of Pharmacology, University Medical School, Pecs, Hungary **Intracerebral neurotransmitters and conditioned reflex performance.** Activitas Nervosa Superior (Praha). 19(2):152-153, 1977.

In a paper delivered at the Second International CIANS Congress (Prague), effects of intracerebrally injected carbachol, nicotine, atropine and noradrenaline on an alimentary conditioned reflex of the cat were studied. The systems investigated were an emotional circuit responsible for the rage reaction of the cat, comprising the hypothalamus and the nonspecific part of the thalamus; and the limbic system. Results show that the conditioned reflex performance was unequivocally inhibited by carbachol stimulation of the anterior hypothalamus or the intralaminar nuclei or the thalamus. 3 references.

001344 Decsi, Laszlo; Nagy, Julia. Institute of Pharmacology, Medical University, P.O. 99, H-7643 Pecs, Hungary **Adrenergic modulation of a cholinergic emotional reaction in the cat's thalamus.** Psychopharmacology (Berlin). 54(3):303-305, 1977.

A study of direct carbachol stimulation of the intralaminar nuclei of the cat thalamus indicates that adrenergic modulation of cholinergic reactions in the CNS is a principle of more general validity than has been assumed. Direct carbachol stimulation of the intralaminar nuclei of the thalamus evokes an affective defense reaction in the cat. Pretreatment of the region with noradrenaline inhibited the reaction in a dose related manner. Phenylephrine was ineffective in this respect while isoprenaline exhibited roughly the same inhibitory action as noradrenaline. The alpha-receptor blocking dihydroergotamine left the inhibitory effect of noradrenaline unaffected while the beta-receptor blocking propranolol abolished it. These findings suggest that the inhibitory effect of noradrenaline on the carbachol induced thalamic emotional reaction is caused by its influence on beta-adrenergic receptors. A similar adrenergic/cholinergic interaction was previously demonstrated for the hypothalamus and red nucleus. 11 references. (Author abstract modified)

001345 Deutsch, J. A.; Walton, Nancy Y. Dept. of Psychology, University of California at San Diego, La Jolla, CA 92093 **Diazepam maintenance of alcohol preference during alcohol withdrawal.** Science. 198(4314):307-309, 1977.

Diazepam maintenance of alcohol preference during alcohol withdrawal was investigated in rats. Rats were fed alcohol via forced intragastric intubation, and diazepam was administered during alcohol withdrawal at doses of 5mg/kg bodyweight. Results indicate that after forced intubation of alcohol, rats showed an increased tendency to self-administer alcohol in a free choice situation, and that diazepam administered during withdrawal served to maintain undiminished such alcohol self-administration. When diazepam dosages were eliminated, the tendency to self-administer alcohol returned to control levels. It is suggested that if diazepam serves to maintain the tendency to choose alcohol, its use in the treatment of alcoholism may be counterproductive. 7 references. (Author abstract modified)

001346 Dolphin, A. C.; Jenner, P.; Sawaya, M. C. B.; Marsden, C. D.; Testa, B. Group N.B., Inserm U 114, College de France, 11 Place Marcelin Berthelot, Paris Cedex 05, France **The effect of bromocriptine on locomotor activity and cerebral catecholamines in rodents.** Journal of Pharmacy and Pharmacology (London). 29(12):727-734, 1977.

To further examine the mechanism by which bromocriptine alters locomotor activity, the roles of both cerebral dopamine (DA) and noradrenaline (NA) were examined in vivo and in vitro in rats and mice using a combination of behavioral and biochemical assessments. The locomotor activity in mice induced by bromocriptine was suppressed by drugs inhibiting both dopaminergic and noradrenergic pre/postsynaptic actions. The onset of locomotor activity was preceded by a period of decreased activity, which lengthened with increasing dose. Both increased and decreased turnover of NA and decreased turnover of DA was shown by measurement of the DA metabolites homovanillic acid, dihydroxyphenylacetic acid (DOPAC) and the noradrenaline metabolite MOPEG-SO4 and following pretreatment of animals with alpha-methyl-p-tyrosine. The increased activity caused by bromocriptine did not correlate with a consistent biochemical change, but the period of behavioral suppression appeared to be associated with an increased NA turnover. Bromocriptine potently inhibited the NA stimulated adenylate cyclase system from mouse limbic forebrain suggesting that the increased in vivo turnover of NA may be due to a postsynaptic receptor blockade. The involvement of cerebral DA receptors was substantiated by the ability of bromocriptine to displace (3H)haloperidol from binding sites in rat striatal preparations. The findings are interpreted as indicating a complex involvement of both NA and DA presynaptic and postsynaptic components in the locomotor activity produced by bromocriptine, possibly due to the involvement of a partial agonist action or an active metabolite. 35 references. (Author abstract modified)

001347 Egbe, Patrick C.; Wray, Samuel R. Dept. of Psychiatry, University of the West Indies, Mona, Kingston 7, Jamaica **Differential attenuation by atropine and d-amphetamine on hyperactivity: possible clinical implications.** Psychopharmacology (Berlin). 54(1):25-30, 1977.

The effects of atropine and d-amphetamine on physostigmine induced hyperactivity in rats were investigated. In-

traperitoneal administration of physostigmine (0.025 to 0.18mg/kg) to rats resulted in significant increases in motor activity as measured with jiggle platforms. Doses of physostigmine 0.2mg/kg or more decreased motor activity. Physostigmine induced hyperactivity was attenuated by atropine (5mg/kg) given before or after physostigmine (0.05mg/kg). On the contrary, d-amphetamine (2mg/kg), given before or after physostigmine significantly potentiated the increase in motor activity. The relevance of the cholinergic system in mediating hyperactive behavior in children is discussed. 41 references. (Author abstract modified)

001348 Eichelman, Burr; Seagraves, Eli; Barchas, Jack. Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **Alkali metal cations: effects on isolation-induced aggression in the mouse.** Pharmacology Biochemistry and Behavior. 7(4):407-409, 1977.

The effects of alkali metal cations on isolation induced fighting in mice were examined. Alkali metal cations were given in varying doses over 14 days to male mice isolated for four weeks prior to testing for isolation induced fighting. Lithium and cesium reduced the duration of isolation induced aggression in a 15 minute test period when compared with controls. Toxicity was evident in the cesium treated, but not the lithium treated mice. No enhancement of aggression was seen in the rubidium treated group. It is concluded that these contrasting effects suggest that different neural systems may be critical in the facilitation or inhibition of these different aggressive paradigms in the mouse. 13 references. (Author abstract modified)

001349 Ervin, Gregory N.; Fink, J. Stephen; Young, Robert C.; Smith, Gerard P. Neurobiology Program, University of North Carolina, Chapel Hill, NC 27514 **Different behavioral responses to L-DOPA after anterolateral or posterolateral hypothalamic injections of 6-hydroxydopamine.** Brain Research (Amsterdam). 132(3):507-520, 1977.

During a study of the effects of 1,3,4-dihydroxyphenylalanine (L-DOPA) on hyperkinesia, it was observed that L-DOPA produced differential behavioral supersensitivity in rats following posterolateral (PL) and anterolateral (AL) hypothalamic injections of 6-hydroxydopamine (6-OHDA): these differences are reported, together with differential patterns of catecholamine (CA) denervation determined by histofluorescent microscopy. L-DOPA produced running and rearing in AL 6-OHDA rats and oral stereotypies in PL 6-OHDA rats. Since the same dose of L-DOPA had no behavioral effect in vehicle injected rats, the responses to L-DOPA of both AL and PL 6-OHDA rats are examples of behavioral supersensitivity. The major regions of CA denervation in AL 6-OHDA rats were neocortex, hippocampus, limbic forebrain, anteromedial striatum and anterolateral hypothalamus. PL 6-OHDA had these same areas denervated and, in addition, had severe denervation of the entire striatum, parts of the amygdala and thalamus, and of the posterolateral hypothalamus. It is concluded that the supersensitive behavioral response to a fixed dose of L-DOPA is determined by the pattern and/or extent of CA denervation. 20 references. (Author abstract modified)

001350 Etscorn, Frank. George Peabody College for Teachers, Nashville, TN 37203 **Illness-induced aversion learning in a desert species of rodent (Acomys cahirinus).** Physiological Psychology. 5(3):336-338, 1977.

Forty nine adult spiny mice (Acomys cahirinus) were made ill by a toxic injection of lithium chloride (US) after six sessions of baseline drinking to determine if the spiny mouse was able to form an illness induced aversion to a novel taste stimulus such as sucrose solution. The injections were made 30 min. after the mice had drunk from a novel sucrose solution (CS). Two days later, the animals were tested for the presence of aversions by offering them a simultaneous choice of drinking either sucrose solution or plain water. The sucrose drinking, illness contingent animals demonstrated significant aversions to the sweet solution when compared to controls. It is concluded that the spiny mouse is capable of learning an illness induced aversion to sucrose solution following one conditional pairing of the sweet liquid and lithium induced illness. 19 references. (Author abstract modified)

001351 Ettenberg, Aron; Milner, Peter M. Dept. of Psychology, McGill University, Montreal, Quebec, Canada **Effects of dopamine supersensitivity on lateral hypothalamic self-stimulation in rats.** Pharmacology Biochemistry & Behavior. 7(6):507-514, 1977.

In a study on the effects of dopamine supersensitivity on lateral hypothalamic self-stimulation in the rat, dopamine (DA) receptor supersensitivity was demonstrated by potentiated d-amphetamine stereotypy after a 3 day treatment regimen in which the DA receptor blocker pimozide (4.0mg/kg) was administered twice daily. Similarly induced DA supersensitivity produced a significant increase in the rate of lever pressing for lateral hypothalamic (LH) intracranial self-stimulation (ICSS) and a significant decrease in ICSS thresholds. No change from pretreatment baselines was observed in vehicle treated control animals. Following 3 day treatment with the noradrenaline (NA) and DA receptor blocker, haloperidol (4.0mg/kg twice daily), a single injection of the alpha-adrenergic agonist clonidine (0.15mg/kg) caused increased running behavior. In contrast clonidine decreased running in rats pretreated with chronic pimozide or vehicle. These results indicate an increase in the sensitivity of central NA receptors following chronic haloperidol but not chronic pimozide. Taken together, these findings were interpreted as a potentiation in the reinforcing properties of LH/ICSS after chronic pimozide treatments due to increases in the sensitivity of DA and not NA receptors. 39 references. (Author abstract)

001352 Evered, M. D.; Fitzsimons, J. T.; De Caro, G. Physiological Laboratory, University of Cambridge, Cambridge, England **Drinking behaviour induced by intracranial injections of eledoisin and substance P in the pigeon.** Nature (London). 268(5618):332-333, 1977.

Drinking behavior induced by intracranial injections of eledoisin and substance P in the conscious pigeon is reported. Intracranial cannulae were implanted stereotaxically; only one drug was tested per day, with a 2 day rest between tests. Drugs injected were eledoisin, eledoisin related peptide, substance P, Asp1Ile5-angiotensin II, arginine vasotocin, vasopressin, bradykinin, and L-glutamate. Intracranial injections of as little as 10 to the minus 11 mol ledoisin consistently caused pigeons to drink water. Volume of water consumed was dose dependent and large. When the relative potencies of angiotensin and eledoisin were compared, it was found that on a molecule per molecule basis eledoisin was only about one order of magnitude less potent than angotensin II. Though less active, eledoisin related peptide and substance P also caused drinking behavior. Other tested drugs elicited no significant effects. 11 references.

001353 File, Sandra E. Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Effects of two anxiolytics on distraction, habituation and dishabituation.** Pharmacology Biochemistry & Behavior. 7(2):105-109, 1977.

The effects of ethanol and chlordiazepoxide on distraction, habituation, and dishabituation as determined by the effects of tone stimuli on licking behavior in rats were studied. Ethanol and chlordiazepoxide produced significantly faster habituation, a result that could not be attributed to changes in the baseline response rate or to differences in the initial distraction to the tone. All animals showed 24 hour retention to the tone when they were tested in the same state in which they were habituated. There was transfer of habituation between drugged and undrugged states for rats injected with chlordiazepoxide, but rats habituated undrugged showed no retention if tested after injections of ethanol. Chlordiazepoxide impaired the specificity with which the physical parameters of the stimulus were coded. Ethanol improved the specificity of coding. Neither drug affected dishabituation. 18 references. (Author abstract modified)

001354 Flaherty, Charles F.; Lombardi, Bruce R.; Kapust, Jeffry; D'Amato, M. R. Psychology Dept., Busch Campus, Rutgers University, New Brunswick, NJ 08903 **Incentive contrast undiminished by extended testing, imipramine, or chlordiazepoxide.** Pharmacology Biochemistry and Behavior. 7(4):315-322, 1977.

Implications of the various theoretical interpretations of contrast in the context of a paradigm in which both positive and negative contrast occur reliably were investigated. In three experiments rats were given alternating 1 minute access periods to two tubes containing sucrose solutions. When the tubes contained disparate concentrations (32% versus 4%), lick rate was higher for the 32% solution than it was when both tubes contained 32% (a positive contrast effect) and less for 4% than when both tubes contained 4% (a negative contrast effect). Similar but generally less pronounced contrast effects were obtained in latency to initiate drinking. These contrast effects showed no sign of diminution with repeated exposure. They were not greatly influenced by injections of imipramine or chlordiazepoxide, nor by deprivation conditions. It is concluded that these results support an explanation of simultaneous contrast in terms of sensory/perceptual processes rather than in terms of generalization decrement or emotional responses. 33 references. (Author abstract modified)

001355 Flannigan, Kelly P.; Whishaw, Ian Q. University of Lethbridge, Lethbridge, Alberta T1K 3M4, Canada **The effects of some pharmacological agents on the duration of immobility shown by rabbits placed in various postures.** Bulletin of the Psychonomic Society. 10(6):499-502, 1977.

Neurological mechanisms governing immobility and the effects of some pharmacological agents on the duration of immobility shown by rabbits placed in various postures were investigated. Dutch belt rabbits remained immobile for longest durations in a back, shortest durations in a sitting, and for intermediate durations in side and front postures. Although atropine and chlorpromazine prolonged and eserine and amphetamine decreased immobility durations, the relative relation of posture to immobility duration was maintained. The drug treatments also affected the duration of spontaneously occurring periods of immobility in a way similar to that observed with induced immobility. There was an inverse relation between body core temperature and immobility duration. The results are discussed in relation to the relative contribution made by central and peripheral factors to the maintenance of immobility. 11 references. (Author abstract modified)

001356 Ford, R. D.; Rech, R. H. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Acute and chronic effects of general CNS depressants on several behavioral tests in rats.** Pharmacologist. 19(2):175, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of several CNS depressants on behavioral tests in rats was reported. After intraperitoneal (ip) injection into animals trained on a fixed interval (FI) schedule for food reinforcement: 1) diazepam increased response rate up to 290%; 2) pentobarbital increased response rate up to 146%; 3) methaqualone increased response rate up to 129%; and 4) alcohol increased response rate up to 114%. Higher doses for each drug decreased rates relative to vehicle controls. Other FI trained rats were made polydipsic to 5% alcohol by intermittent delivery of food pellets in home cages. Weekly ip doses of alcohol reduced response rates markedly at first, but tolerance developed slowly over 4 months. Testing of the other drugs at this time showed crosstolerance, with dose/response curves being shifted to the right. However, no tolerance to the rate enhancing effects of the drugs was noted. Other rats trained to walk the rotarod received 10% ethanol orally over 2 to 3 months. Tolerance to ip alcohol measured as decreased duration of rotarod impairment was less impressive than was crosstolerance to the other drugs. Other rotarod trained animals were tolerant to diazepam effects and crosstolerant to methaqualone after a few weeks of daily diazepam. It is suggested that tolerance and crosstolerance to diazepam, pentobarbital, and methaqualone develop more readily than does tolerance to alcohol. (Author abstract modified)

001357 Fox, Robert A. San Jose State University, San Jose, CA **Poison aversion and sexual behavior in the golden hamster.** Psychological Reports. 41(3, Part 1):993-994, 1977.

Disruption of 10 male hamsters sexual behavior following pairing of lithium chloride poisoning and female vaginal secretion was studied using male and female hamsters that had been isolated for 5 wk prior to poisoning. Sniff/lick latencies were longer for poisoned males than for controls but mount times and intromission times were unaffected. These results are consistent with cue uniqueness effects and also demonstrate conditioned aversion to olfactory sexual cues is not necessarily sufficient to disrupt the male sexual response sequence. 5 references. (Author abstract)

001358 Frances, Henriette; Simon, P. Dept. de Pharmacologie, Faculte de Medecine, Pitie-Salpetriere, 91 Bd. de l Hopital, F-75634 Paris Cedex 13, France **Influence of some neuro-psychotropic drugs on the behavioural modifications induced by 3-acetylpyridine in rats.** Progress in Neuro-Psychopharmacology. 1(3/4):297-300, 1977.

The influence of some neuropsychotropic drugs on the functional disorders induced in rats by 3-acetylpyridine, a nicotinamide antimetabolite, were investigated. 3-Acetylpyridine (65mg/kg i.p.)induced rolling, hypermotility, flatness, and tremors in rats. In an attempt to study several neuropsychotropic drugs as possible antagonists of the symptoms, it was found that: 1) amphetamine improved all symptoms except tremors; 2) pilocarpine and oxotremorine reduced only rolling; 3) idrocilamide, baclofen and diazepam reduced only tremors; and 4) no effect was observed for the studied doses of L-dopa, apomorphine, L-5HTP, methysergide, picrotoxin

and atropine. It is noted that the myorelaxant properties of idrocilamide, baclofen and diazepam would represent the basic effect and could be used when screening for a new minor tranquilizer as a simple, rapid, and inexpensive test. It is speculated that the site of action of the effective drugs may be related to an action on catecholaminergic, cholinergic, or GABAergic synaptic levels along the pathways involved between lesions and periphery. 6 references. (Author abstract modified)

001359 Frederickson, R. C. A.; Slater, I. H.; Dusenberry, W. E.; Hewes, C. R.; Jones, G. T.; Moore, R. A. Lilly Research Laboratories, Eli Lilly & Co., Indianapolis, IN 46206 **A comparison of thalidomide and pentobarbital -- new methods for identifying novel hypnotic drugs.** Journal of Pharmacology and Experimental Therapeutics. 203(1):240-251, 1977.

The effects of thalidomide and pentobarbital in cats and in rodents were compared. In a dose range that did not produce ataxia, thalidomide increased slow-wave sleep and rapid eye movement sleep in cats and rats. Pentobarbital had hypnotic activity in the same dose range but produced ataxia. Thalidomide reduced spontaneous activity of both mice and rats over a wide oral dose range; however, this effect plateaued at a level of activity well above the complete inactivity produced by high doses of pentobarbital. Pentobarbital, at doses up to 10 times the hypnotic dose range, prevented audiogenic seizures in physically dependent rats withdrawn from sodium barbital, but thalidomide did not substitute for barbiturates even at doses 30 times those that increased sleep. Thalidomide, but not pentobarbital, enhanced the sleep producing effect of electrical stimulation of the basal forebrain in cats. It is suggested that thalidomide probably has a mechanism of action different from that of pentobarbital and that this may involve the activation of a sleep center in the forebrain. It is further suggested that the differences in the effects of thalidomide and pentobarbital revealed by these tests may provide a useful means of screening new compounds for thalidomidelike hypnotic activity. 28 references. (Author abstract modified)

001360 Fuxe, K.; Everitt, B. J.; Hokfelt, T. Dept. of Histology, Karolinska Institutet, Stockholm, Sweden **Enhancement of sexual behavior in the female rat by nicotine.** Pharmacology Biochemistry & Behavior. 7(2):147-151, 1977.

The effects of nicotine, mecamylamine, various dopamine (DA) agonists, DA antagonists, and a serotonin (5-hydroxytryptamine, 5-HT) agonist, alone and in various combinations, on the sexual behavior of castrate, estrogen treated female rats were studied. Nicotine produced a significant increase in sexual receptivity which was: 1) blocked by pretreatment with mecamylamine; 2) not increased by pimozide although pimozide alone had the same effect on sexual behavior as did nicotine; 3) slightly increased by d-lysergic acid diethylamide (d-LSD), which increased sexual behavior when given alone; 4) not further increased by apomorphine, which increased sexual behavior when given alone; and 5) not blocked by sulpiride. Mecamylamine did not block the increases in sexual behavior induced by apomorphine of d-LSD. It is suggested that the effects of nicotine on sexual behavior are mediated by a central, nicotinelike cholinergic receptor. The relationship between this receptor and DA and 5-HT pathways known to exert inhibitory influences on receptivity in the female rat is discussed. 26 references.

001361 Gay, Patricia E.; Potter, Larry S.; Consalvi, John A., Jr.; Leaff, Russell C. Camden College of Arts and Sciences, Rutgers University, Camden, NJ 08120 **The effects of d-amphetamine on prey killing and prey eating in the rat and mouse.** Bulletin of the Psychonomic Society. 10(5):385-388, 1977.

The relation of d-amphetamine inhibition of prey killing and prey eating to anorexia is explored in rats and mice. d-Amphetamine inhibited mouse, frog, and cricket killing in the rat and cricket killing in the laboratory mouse. Feeding on the same prey was also inhibited, but required a lower dose of the drug. While the anoxeric effects of d-amphetamine may contribute to the drug's inhibition of prey killing, other physiological actions of the drug also appear to be involved. 16 references. (Author abstract modified)

001362 Gehlhausen, Terry C.; Zabik, Joseph E. Section on Pharmacology, Indiana University School of Medicine, Bloomington, IN 47401 **A biochemical and behavioral analysis of chronic alcohol consumption by rats.** Pharmacologist. 19(2):138, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the biochemical and behavioral effects of chronic alcohol consumption by rats was reported. The rats were trained to consume their entire daily intake of fluid in a 1 hr period. After stable water intake baselines were achieved, aqueous ethanol solutions were substituted for the water. The volume consumed was inversely related to the concentration of ethanol, resulting in a uniform daily intake of ethanol. The terminating factor may have been pharmacological impairment rather than satiety; animals on the higher concentrations were depressed when removed from the drinking cages. Lickometer studies confirmed the patterns of consummatory behavior observed in the free drinking situation, especially in terms of erratic performance in the early days of alcohol exposure. After 3 weeks of chronic ethanol exposure, brain serotonin (5-hydroxytryptamine) levels were elevated. It is proposed that this system is amenable to use as a test procedure for studying the interactions of drugs and other compounds with chronic alcohol ingestion. (Author abstract modified)

001363 Gerald, Michael C. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Effects of amphetamine on endurance performance and muscle weakness in rats.** Pharmacologist. 19(2):174, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of dextroamphetamine and levoamphetamine on endurance performance and muscle weakness in the rat was reported. Endurance performance was measured on a treadmill, while muscle weakness was evaluated by rotarod. At a treadmill speed of 18.8meters/min, 0.312mg/kg to 5mg/kg of dextroamphetamine administered 15 min prior to testing increased the endurance performance of untrained rats by up to 67%, while 7.5mg/kg to 10mg/kg of the drug reduced running times by up to 47%. Levoamphetamine reduced endurance performance by up to 58%. At treadmill speeds of 10.7meters/min to 26.8meters/min, 2.5mg/kg of dextroamphetamine increased endurance performance by up to 100%, while 10mg/kg of dextroamphetamine reduced endurance performance by up to 47%. Both amphetamine isomers impaired rotarod performance in a dose dependent manner. Neostigmine attenuated dextroamphetamine neurotoxicity. Repeated daily doses of 30mg/kg dextroamphetamine daily reduced the incidence of rotarod failures from 75% on day 1 to 10% on day 8. The results are in agreement with in

vitro observations demonstrating the dose dependent biphasic effects of amphetamine on muscle contractions and suggest that amphetamine induced muscle weakness may be in part peripherally mediated. 1 reference. (Author abstract modified)

001364 Gildea, M. L.; Bourn, W. M. School of Pharmacy, Northeast Louisiana University, Monroe, LA 71203 **Effect of barbiturate withdrawal on pentylenetetrazol seizure threshold.** Communications in Psychopharmacology. 1(2):123-129, 1977.

The effect of barbiturate withdrawal on the pentylenetetrazol seizure threshold was measured in an experiment in which rats with permanently implanted cortical electrodes were given increasing doses of sodium barbital over a 5 week period until a daily dose of 400mg/Kg was attained and continued for 1 week. The barbiturate was then discontinued and the rats were challenged with intravenous pentylenetetrazol twice during the withdrawal period. Cortical spiking occurred following a significantly lower dose of pentylenetetrazol in withdrawn rats as compared to controls. In addition, it was observed that the spiking occurred at a much lower dose than that required to produce clonic convulsions. 9 references. (Author abstract modified)

001365 Glick, S. D.; Cox, R. D.; Jerussi, T. P.; Greenstein, S. Department of Pharmacology, Mount Sinai School of Medicine, CUNY, Fifth Ave. and 100th St., New York, NY 10029 **Normal and amphetamine-induced rotation of rats on a flat surface.** Journal of Pharmacy and Pharmacology (London). 29(1):51-52, 1977.

Amphetamine induced rotation on a flat surface and in a bowl was studied in naive female Sprague-Dawley rats. The rats were given (+)-amphetamine and placed in either a spherical plexiglass bowl 30.5cm in diameter or in plexiglass box 30.5cm x 30.5cm. A week later, the same rats were again given (+)-amphetamine and placed in the other apparatus. The mean number of rotations was 42 per hr for the bowl and 37 per hr for the flat surface, a difference which was not significant. It is concluded that isolation in any enclosed apparatus is sufficient for observing drug induced rotation in the normal animal. Drug naive rats made 42.5rotations per day on the flat surface without being given any drug, thus showing that rotation is a normal component of rat behavior. 16 references.

001366 Godschalk, Moshe; Dzoljic, Mihailo R.; Bonta, Ivan L. Department of Pharmacology, Faculty of Medicine, Erasmus University Rotterdam, P.O. Box 1738, Rotterdam, The Netherlands **Slow wave sleep and a state resembling absence epilepsy induced in the rat by gamma-hydroxybutyrate.** European Journal of Pharmacology (Amsterdam). 44(2):105-111, 1977.

The effect of gamma-hydroxybutyrate on sleep stages, electrogram patterns and behavior was investigated in the rat. Results show that gamma-hydroxybutyrate may induce slow wave sleep in the dose range of 50 to 100mg/kg. A dose of 200mg/kg induces a hypersynchronous, bilaterally symmetrical electrocorticogram pattern which is different in amplitude and frequency distribution from normally occurring high amplitude patterns. When the hypersynchrony occurred in bursts, rats displayed a sudden arrest of motor behavior. Convulsions were not induced. These results, in conjunction with previous studies, suggest gamma-hydroxybutyrate might play a role in the etiology of absence epilepsy in man. 16 references.

001367 Grabowska-Anden, Maria. Dept. of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg, Sweden **Modification of the amphetamine-induced stereotypy in rats following inhibition of the noradrenaline release by FLA 136.** Journal of Pharmacy and Pharmacology (London). 29(9):566-569, 1977.

The influence of noradrenaline (NA) on amphetamine induced stereotypy was investigated in rats by examining the effects of FLA-136, which inhibits NA release, and of yohimbine, which enhances NA synthesis and utilization, on amphetamine induced stereotypy. FLA-136 produced a significant potentiation of amphetamine induced stereotypy, while yohimbine inhibited amphetamine induced stereotypy and abolished the potentiation of amphetamine induced stereotypy produced by FLA-136. The data support the hypothesis that NA has a modulatory influence on amphetamine induced stereotypy. 6 references.

001368 Grilly, David M. Dept. of Psychology, Cleveland State University, Cleveland, OH 44115 **Rate-dependent effects of amphetamine resulting from behavioral competition.** Biobehavioral Reviews. 1(2):87-93, 1977.

A hypothesis that most of the rate dependent effects and exceptions are the result of interaction and competition with other amphetamine induced activities, e.g. locomotion and stereotypy, is reviewed and discussed. The evidence strongly suggests that such a competing response process does occur, particularly at higher dose levels. The process is interpreted as being consistent with such anomalous results as amphetamine's lack of a reliable effect on high rate bursting in timing schedules, the differential effects of amphetamine on the low rate timing behavior of pigeons and rats, the lack of an enhancing effect of amphetamine on low rate behavior suppressed by aversive stimulation, and the apparent lack of systematic effect of amphetamine on very low rate behavior. 48 references. (Author abstract)

001369 Gromova, E. A. Institute of Biophysics of the USSR Academy of Sciences, Puschino on Oka, USSR **Role of the brain monoamine system in learning on various emotional reinforcements.** Activitas Nervosa Superior (Praha). 19(2):127-128, 1977.

In a paper delivered at the Second International CIANS Congress (Prague), the hypothesis that the monoamine system is the neuroanatomical substrate of interaction between emotions and memory was investigated. In experiments with food reinforcement, daily treatment of the rats with 5-hydroxytryptophan (5-HTP) resulted in considerable facilitation of learning and greater stability of the reaction. PCPA, an inhibitor of 5-HTP synthesis, had an opposite effect and a precursor of noradrenalin, DOPA, did not noticeably affect speed of learning. When treating the animals with the same substances in the course of learning with negative reinforcement, the period of learning became longer under 5-HTP and shorter with PCPA. These results support the conception that positive and negative systems of reinforcement have a different neurochemical nature.

001370 Grove, L.; Wilson, M.; Bedford, J. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Effects of diazepam and d-amphetamine on food competition in Rhesus monkey.** Pharmacologist. 19(2):228, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of diazepam and dextroamphetamine on food competition in four juvenile Rhesus monkeys was reported. Food competition

tests were performed with all possible subject pairs and when all subjects were housed in one cage. Administration of diazepam to both subjects in the paired test, to all members in the group test, or to only the more dominant animal of a pair, produced an increase in the proportion of food obtained by submissive animals. Administration of dextroamphetamine to both subjects or to the more dominant animals in the paired test resulted in an even greater increase in food capture by the less dominant animal. Treatment in the group setting resulted in the more submissive subjects obtaining all of the food. Both of these subjects died within 24 hr. It is posited that the behavioral effect of a drug is influenced by the social dominance of the subject. (Author abstract modified)

001371 Handley, George W. Ohio State University, Columbus, OH **Effects of methylphenidate on acquisition and subsequent performance of successive discrimination reversals.** Psychological Reports. 41(2):543-546, 1977.

The short-term and long-term effect of methylphenidate on acquisition and subsequent performance of successive discrimination reversals were studied in 20 rats trained to bar press for sucrose solution in the presence of one of two stimulus conditions. On each of six daily training sessions the reward value of the stimuli was reversed, and 20 min prior to the second reversal, the subjects received an i.p. injection of either isotonic saline, 2 mg/kg, 4 mg/kg, or 8 mg/kg of methylphenidate. The performance of drugged subjects was superior on reversal 2. In the 2 mg/kg condition this effect persisted over reversals 2 to 6, indicating that more than a transient performance effect was induced by drug administration. A second study using 16 subjects was conducted to ascertain additional information relative to the effects of the 2 mg/kg dose on short-term and long-term performance. Results supported the contention that this dose level, when administered during early training, produces long-term enhancement of problem-solving. 5 references. (Author abstract modified)

001372 Harris, R. Adron; Snell, Diane; Loh, Horace H. Dept. of Pharmacology, University of California, San Francisco, CA 94143 **Stereoselective effects of 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) on schedule-controlled behavior.** Pharmacology Biochemistry and Behavior. 7(4):307-310, 1977.

The effects of stereoisomers of 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) were studied using rats responding under a fixed interval 2 min schedule of food presentation. All three drugs decreased average rates of responding in a dose related manner, with R-DOM being five to six times more potent than S-DOM but only about 1.2times more potent than R,S-DOM. Relatively high doses of R,S-DOM and S-DOM increased the low response rates occurring at the beginning of the fixed interval and decreased the higher response rates occurring at the end of the interval (rate-dependent effects). These results are discussed in terms of the stereoselective metabolism of DOM and of the structural similarities between R-DOM and the behaviorally active isomer of LSD. 24 references. (Author abstract)

001373 Harry, G. J.; Rosecrans, J. A. Medical College of Virginia, Richmond, VA 23298 **The pharmacological effects of fetal and neonatal exposure to naltrexone in the rat.** Pharmacologist. 19(2):143, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the pharmacological effects of fetal and neonatal exposure to naltrexone in the rat was reported. Pregnant rats were exposed to naltrexone via drinking water throughout either the prenatal period or both the prenatal and postnatal periods. Rat pups receiving naltrexone prenatally exhibited less methadone induced aversion and morphine induced antinociception. Rat pups receiving naltrexone both prenatally and neonatally exhibited similar but less evident effects. In addition, rats of both sexes born to mothers receiving naltrexone prenatally and postnatally exhibited less of a conditioned emotional response to an auditory conditioned shock. (Author abstract modified)

001374 Harto, N. E.; Howard, J. L.; Leander, J. D.; Rohrbach, K. R.; Pollard, G. T.; Maxwell, R. A. Department of Pharmacology, Wellcome Research Laboratories, Research Triangle Park, NC 27709 **Effects of d-amphetamine on a multiple fixed-ratio, fixed-interval schedule of food reinforcement in the cat.** Pharmacologist. 19(2):227, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of dextroamphetamine on operant responding in cats trained on a multiple fixed-ratio (FR), fixed-interval (FI) schedule of food reinforcement was reported. When administered intraperitoneally immediately prior to testing, dextroamphetamine produced a dose dependent decrease in FR responding rates. Overall FI response rates were increased by low doses of the drug but decreased by higher doses. Within the FI, dextroamphetamine produced a dose dependent increase in the very low rates of responding which occurred early in each interval, and a decrease in the high rates of responding during the terminal portions of the interval. These effects of dextroamphetamine within the FI yielded a constant rate of responding at higher doses. These results indicate that dextroamphetamine's effects on operant responding in the cat are similar to those in other species. (Author abstract modified)

001375 Haycock, John W.; Van Buskirk, Roderick; Gold, Paul E. Dept. of Psychobiology, School of Biological Sciences, University of Calfornia, Irvine, CA 92717 **Effects on retention of posttraining amphetamine injections in mice: interaction with pretraining experience.** Psychopharmacology (Berlin). 54(1):21-24, 1977.

The effects of d-amphetamine on retention of one trial inhibitory avoidance training in mice were investigated. Water deprived mice were pretrained to lick from a water spout at the end of a darkened compartment. Footshock was administered during licking after 4, 6, or 7 days of pretraining. Retention performance was measured 24 hours after training. The effects on memory of posttraining amphetamine varied not only with amphetamine dose but also with the amount of pretraining. The results are consistent with the view that posttraining treatments may affect memory storage processes by interacting with training related arousal levels. 20 references. (Author abstract modified)

001376 Herink, J.; Hrdina, V.; Kvetina, J. Purkyne Medical Research Institute and Faculty of Pharmacy, Hradec Kralove, Czechoslovakia **Effect of some centrally active compounds on aggressive behaviour in septal rats.** Activitas Nervosa Superior (Praha). 19(3):227, 1977.

In a paper presented at the second international CIANS congress, the interaction of the effects of atropine, 3-quinuclidyl benzilate, and diazepam with septal lesions in rats were investigated. Shock elicited fighting behavior was elicited in 280 male rats. The rats were divided into three groups, operated,

sham operated, and controls. The septal group showed higher sensitivity to the effect of the anticholinergics. The different septal sensitivity of septal rats could be due to an intervention of the lesions in the specific neuronal mechanism. It is suggested that this could be localized outside the septum and some of the pharmacological effects may be ascribed to a drug action outside the lesioned area.

001377 Hetta, J. Institute of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **Effects of morphine and naltrexone on sexual behaviour on the male rat.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):53, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea Sweden, August 15-17, 1977, the effects of morphine and naltrexone on sexual behavior were studied in intact male rats tested in copulatory tests with estrous females. Morphine (2.5mg/kg) significantly decreased the number of mounts, but the number of intromissions was not affected, giving a higher intromission ratio. Morphine (5mg/kg) decreased the number of animals showing mounting activity, gave fewer mounts, and lowered the intromission ratio. Naltrexone increased the percentage of rats that ejaculated. The results suggest an inhibitory influence of morphine on sexual behavior of the male rat and that endorphins could be involved in the regulation of ejaculation.

001378 Hirschhorn, Ira D. Department of Pharmacology, New York College of Podiatric Medicine, 53 East 124 St., New York, NY 10035 **Pentazocine, cyclazocine, and nalorphine as discriminative stimuli.** Psychopharmacology (Berlin). 54(3):289-294, 1977.

In a study of the stimulus properties of pentazocine, cyclazocine, and nalorphine, three narcotic antagonists that also have analgesic activity of their own, each drug was used as a discriminative stimulus for a separate group of rats. Depression of one level resulted in food reinforcement following the administration of drug, and the opposite lever was reinforced after saline. Each drug readily acquired control of discriminated responding. The specific narcotic antagonist, naloxone, which antagonizes many of the effects of pentazocine, cyclazocine, and nalorphine, also antagonized the discrimination of these drugs. Stimulus generalization tests to each other narcotic antagonist, d-amphetamine, morphine, and LSD, showed that each narcotic antagonist has highly specific stimulus properties. Clear generalization occurred only to pentazocine and cyclazocine in the nalorphine/saline group, but neither cyclazocine nor pentazocine generalized to nalorphine. 19 references. (Author abstract modified)

001379 Hitzemann, R. J.; Tseng, L. F.; Hitzemann, B. A.; Sampath-Khanna, S.; Loh, H. H. Department of Pharmacology, University of California, San Francisco, CA 94143 **Effects of withdrawal from chronic amphetamine intoxication on exploratory and stereotyped behaviors in the rat.** Psychopharmacology (Berlin). 54(3):295-302, 1977.

In a study of the effects of withdrawal from chronic amphetamine intoxication on exploratory and stereotyped behaviors in the rat, rats were administered d-amphetamine twice daily on a weekly increasing staircase schedule. On days 1, 7, 14, and 28 after the last injection of amphetamine the animals were challenged with 1 and 3mg/kg of d-amphetamine and their behavior was observed. The 7, 14, and 28 day withdrawn animals required less amphetamine than controls to induce stereotyped behaviors. However, it was found that withdrawn animals and control animals were equally sensitive to the effects of apomorphine. Reserpine pretreatment eliminated the differences between control and withdrawn animals. Alpha-methyl tyrosine pretreatment blocked the effects of 1 but not 3mg/kg of d-amphetamine in the withdrawn animals. Possible chemical mechanisms underlying the change in amphetamine sensitivity in the withdrawn animals are discussed. 22 references. (Author abstract modified)

001380 Holmgren, Bjorn; Urba-Holmgren, Ruth. Centro Nacional de Investigaciones Cientificas, Apartado 6990, La Habana, Cuba **Cholinergic mechanisms involved in head-shaking of infant rats.** Pharmacology Biochemistry & Behavior. 7(6):493-499, 1977.

Central cholinergic mechanisms involved in d-amphetamine induced head shaking were explored in 9-day-old albino rats using anticholinergic, anticholinesterase and cholinomimetic drugs. Scopolamine (5mg/kg) blocks both spontaneous and d-amphetamine induced head shaking. Physostigmine (0.10mg/kg), but not neostigmine, increases d-amphetamine induced head shaking up to 400%. Pilocarpine (1 to 10 mg/kg) per se induces head shaking and strongly potentiates the amphetamine head shaking effect. Cholinergic/catecholaminergic interactions in the central nervous system are discussed in relation to the expression of head shaking. A cholinoceptive modulation of rhythmical descending and reciprocally organized vestibulospinal inputs on motoneurones innervating head and neck muscles is considered a reasonable hypothesis to explain the results. 56 references. (Author abstract modified)

001381 Hynes, Martin D.; Lal, Harbans. Department of Pharmacology and Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Naloxone interaction with neuroleptic-induced suppression of narcotic withdrawal.** Pharmacologist. 19(2):170, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of naloxone on suppression of narcotic withdrawal by various narcotics and neuroleptics was reported. Narcotic dependence was established in rats by continuous intravenous infusion of morphine in increasing concentrations. Termination of the infusion resulted in the occurrence of body shakes. Morphine, methadone, and fentanyl blocked withdrawal body shakes in a dose dependent manner. Haloperidol, benperidol, and azaperone were also effective in reducing body shakes in a dose dependent manner. Trifluoperazine and chlorpromazine reduced withdrawal body shakes only at sedative doses. The dextrorotatory isomer of butaclamol was effective in reducing body shakes; its levorotatory isomer was ineffective. The antiwithdrawal action of morphine, haloperidol, benperidol, and azaperone, but not that of chlorpromazine, trifluoperazine, and butaclamol, was antagonized by naloxone. Whereas naloxone antagonism of the narcotic drugs was dose dependent and complete, the antagonism of the neuroleptic drugs reached a plateau before reaching complete reversal. (Author abstract modified)

001382 Inubushi, Shikio; Koizumi, Takahiko; Tanaka, Michio; Torii, Shizuo 1st Dept. of Physiology, School of Medicine, Toho University, Omori, Tokyo, Japan **Effects of L-5-hydroxytryptophan on sleep-wakefulness cycles in cats.** Journal of the Medical Society of Toho University (Tokyo). 24(2):246-251, 1977.

The effects of L-5-hydroxytryptophan (L-5-HTP) on sleep-wakefulness cycles in two cats with chronically implanted

electrodes for recording the electroencephalogram, the nuchal electromyogram, and the electrooculogram were studied. Polygraph recordings were obtained from each cat for a 24 hour period every seventh day for a 10 month period. During these experiments animals received either placebos or L-5-HTP (0.5, 1.0, 2.0, 4.0mg/kg) orally prior to recording. Two mg/kg of L-5-HTP produced a decrease in wakefulness and an increase in both NREM and REM sleep. Four mg/kg also increased REM sleep, but did not cause any consistent changes in either wakefulness or NREM sleep. 11 references. (Author abstract modified)

001383 Jacobs, Barry L.; Trulson, Michael E.; Stark, Arlene D.; Christoph, Greg R. Department of Psychology, Princeton University, Princeton, NJ 08540 **Comparative effects of hallucinogenic drugs on behavior of the cat.** Communications in Psychopharmacology. 1(3):243-254, 1977.

Comparative effects of hallucinogenic drugs on behavior of the cat were studied in cats administered LSD and functionally related hallucinogen, such as psilocybin, STP, psilocin, DMT and mescaline. Results indicate that all of the compounds produced a significant increase in the frequency of occurrence of at least one of the behaviors of limb flick, abortive groom, investigatory play, and hallucinatory like behavior in the cat. The minimal doses necessary to produce the same behavioral effects closely correspond to the relative potency of these compounds for human hallucinogenesis. Thus it is concluded that the behaviors studied should serve as an animal model for studying the parameters and physiological bases of this class of hallucinogens. 15 references.

001384 Jankowska, E.; Lundberg, A.; Rudomin, P.; Sykova, E. Department of Physiology, University of Goteborg, Goteborg, Sweden **Effects of 4-aminopyridine on transmission in excitatory and inhibitory synapses in the spinal cord.** Brain Research (Amsterdam). 136(2):387-392, 1977.

In view of the likelihood that 4-aminopyridine (4-AP) interacts with basic synaptic mechanisms, its effect on synaptic transmission in the cat CNS was investigated. Evidence is presented that 4-AP markedly facilitates transmission in excitatory as well as inhibitory pathways in the spinal cord, and that it acts by increasing postsynaptic potentials in both kinds of synapses, presumably by a presynaptic effect. Speculations are offered regarding the manner in which the drug has a regulatory effect in the CNS. 12 references.

001385 Jarbe, T. U. C. University of Uppsala, Department of Psychology, P.O. Box 227, S-75104 Uppsala, Sweden **Alcohol-discrimination in gerbils: interactions with bemegride, DH-524, amphetamine, and delta9-THC.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 227(1):118-129, 1977.

Possible generalization or antagonism of alcohol induced discrimination by bemegride, the imidazoline derivative DH-524, amphetamine, or delta9-THC was investigated in the mongolian gerbil (Meriones unguiculatus). Male gerbils (n=15) were trained to discriminate the effects of an injection of alcohol from nondrug condition in a T-maze. Results suggest that none of these drugs substituted for alcohol, nor did the drugs reverse or antagonize the alcohol discrimination, i.e. the gerbils chose the nondrug associated position of the maze after single injections of the test drugs, whereas combinations of alcohol and the test drugs resulted in responding appropriate for the alcohol (training) condition. 40 references. (Journal abstract modified)

001386 Jarbe, T. U. C.; Ohlin, G. Ch. University of Uppsala, Department of Psychology, P.O. Box 227, S-75104 Uppsala, Sweden **Interactions between alcohol and other drugs on open-field and temperature measurements in gerbils.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 227(1):106-117, 1977.

The effect of interaction between alcohol and other drugs on open-field activity and rectal temperature were investigated in the gerbil (Meriones unguiculatus). Open-field activity and rectal temperature were measured in mongolian gerbils when alcohol was combined with bemegride, with the imidazoline derivative DH-524, or with d-amphetamine. None of the drugs reversed the alcohol induced hypothermia, nor was there normalization of the open-field scores. However, alcohol offered protection against bemegride induced convulsion and death. 38 references. (Journal abstract modified)

001387 Jarbe, Torbjorn U. C.; Holmgren, Boel. Department of Psychology, Box 227, University of Uppsala, S-75104 Uppsala, Sweden **Discriminative properties of pentobarbital after repeated noncontingent exposure in gerbils.** Psychopharmacology (Berlin). 53(1):39-44, 1977.

Two groups of gerbils were pretreated with pentobarbital (P-barb) (10 and 20mg/kg) for 20 days before being subjected to drug discrimination training in a T-shaped shock escape maze and the rapidity with which these gerbils acquired the discrimination was compared to that of gerbils that were drug naive until beginning the P-barb discrimination training. The acquisition rates of the respective groups did not differ substantially within each dose level (10 and 20mg/kg), although open-field activity (primarily the rearing scores) differentiated the P-barb and vehicle pretreated animals at both dose levels. The peak effect in rectal temperature, however, was not markedly different after the first and 20th drug exposures, although the temperature effects leveled off earlier during the second recording session. It is concluded that certain parameters (open-field activity) may be changed as a consequence of repeated administrations of P-barb without a significant parallel loss of the cue or stimulus properties of the drug. 43 references. (Author abstract)

001388 Jolicoeur, F. B.; Rondeau, D. B.; Wayner, M. J.; Mintz, R. B.; Merkel, A. D. Institut de Recherches Cliniques de Montreal, Montreal, P.Q., Canada **Barbiturates and alcohol consumption.** Biobehavioral Reviews. 1(3):177-196, 1977.

The effects of phenobarbital on forced consumption of alcoholic and nonalcoholic solutions in water deprived rats were examined. The results indicated that phenobarbital can produce a taste aversion to ethanol solutions but not to nonalcoholic solutions in animals previously acclimated in these solutions. These data suggested a specific pharmacological interaction between the barbiturate and alcohol, and a series of experiments on the effects of phenobarbital on voluntary alcohol consumption in rats was performed. The results of these studies indicate that chronic administration of certain doses of phenobarbital decreases preference for sweetened and nonsweetened 3% and 6% ethanol solutions but does not affect preference for nonalcoholic glucose and saccharin solutions. Similar administration of 30mg/kg amobarbital, 80mg/kg barbital, 2.5mg/kg diazepam, 1.0mg/kg methyprylon, and 10.0mg/kg methaqualone did not alter intakes and preference for a 6% ethanol solution. the apparent specificity of phenobarbital in reducing ethanol consumption suggests a specific interaction between the two drugs. 28 references. (Author abstract modified)

001389 Kallman, M. D.; White, A. C.; Rosecrans, J. A. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Chronic and acute effects of barbital and amphetamine in dopamine depleted rats.** Pharmacologist. 19(2):228, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the acute and chronic effects of barbital and amphetamine in dopamine (DA) depleted rats was reported. DA depletion was accomplished by pretreating the animals intraperitoneally with desmethylimipramine followed by intracisternal injections of 6-hydroxydopamine. Both acute and chronic drug effects were ascertained by response rates on a variable interval operant schedule for a sweetened milk reinforcer. DA depletion did not affect the development of tolerance to chronic administration of barbital or dextroamphetamine. The acute effects of barbital were not altered in DA depleted rats, but the acute effects of dextroamphetamine were enhanced. Changes in response rates were independent of alteration in food intake, since both DA depleted and control animals consumed equal amounts of food daily. Brain amine levels indicated a 67% reduction in striatal DA in the depleted animals while norepinephrine levels were unchanged. (Author abstract modified)

001390 Karmos-Varszegi, Maria; Karmos, G. Institutes of Pharmacology and Physiology, University Medical School, Pecs, Hungary **A comparative study of autonomic, somatic and bioelectric correlates of emotional reactions elicited by cholinergic stimulation of the hypothalamus and the ventral tegmentum.** Activitas Nervosa Superior (Praha). 19(2):123-124, 1977.

In a paper delivered at the Second International CIANS Congress (Prague), a polygraphic analysis of the defensive threat and the stalking attack elicited in freely moving cats by local administration of Carbachol (CCh) into the medial hypothalamus and the ventral tegmentum is presented. The hippocampal and cortical EEG, electrooculogram, electromyogram (EMG) of the neck muscles and the blood pressure were recorded in freely moving cats along with separate registration of growling and hissing. Hypothalamic CCh stimulation produced marked increases in heairtrate and blood pressure lasting far longer than the overt manifestations of the emotional reaction. CCh in the ventral tegmentum produced attacking even in satiated cats. It is suggested that the chemically induced emotional reactions, when their physiological manifestations are quantitatively measured, may serve as good experimental models for pharmacological analysis of psychoactive drugs. 4 references.

001391 Katz, R. J.; Carroll, Bernard J. Dept. of Psychiatry, Mental Health Research Inst., Univ. of Michigan, Ann Arbor, MI 48109 **Effects of chronic lithium and rubidium administration upon experimentally induced conflict behavior.** Progress in Neuro-Psychopharmacology. 1(3/4):285-288, 1977.

The effects of chronic lithium (Li) and rubidium (Rb) administration on behavior suppressed by punishment were studied in male Sprague-Dawley rats. Chronic treatment of rats with Li produced a significant reduction of shock induced suppression of feeding behavior (passive avoidance). Rb caused additional suppression of feeding under the same conditions. Results suggest that the two drugs may affect anxiety processes in opposite directions, and that this may be of clinical significance; given the clinical efficacy of lithium in the control of manic states, it is considered possible that rubidium may be an effective antidepressant. 25 references. (Author abstract modified)

001392 Knoll, Bertha. Dept. of Pharmacology, Semmelweis University of Medicine, Budapest, Hungary **The effect of para-Br-methamphetamine on aggressive behaviour.** Activitas Nervosa Superior (Praha). 19(3):225-226, 1977.

In a paper presented at the second international CIANS congress, the behavioral effects of para-Br-methamphetamine (V-111) on aggressive behavior in rats were examined in a one way active avoidance situation with attention to the drug's serotonergic control of muricide. The effects on muricide of para-chlorphenylalanine (pCPA) and of raphe lesion were compared with both acute and chronic V-111 treatments. Biochemical findings suggest that the inhibition of muricide after acute pharmacological manipulations with V-111 in pCPA pretreated and raphe lesioned rats is probably the consequence of an increased serotonin outflow to the receptors. 8 references.

001393 Kostowski, W.; Jerlicz, Maria; Bidzinski, A.; Hauptmann, Miroslawa. Dept. of Pharmacology and Physiology of the Nervous System, Psychoneurological Institute, 02-957 Warszawa, Poland **Behavioral effects of neuroleptics, apomorphine and amphetamine after bilateral lesion of the locus coeruleus in rats.** Pharmacology Biochemistry and Behavior. 7(4):289-293, 1977.

The behavioral effects of neuroleptics, apomorphine, and amphetamine after bilateral lesion of the locus coeruleus (LC) in rats were investigated. Bilateral lesions of the LC markedly increased susceptibility to the cataleptogenic effects of neuroleptics. The apomorphine induced stereotypy was enhanced in rats with lesioned LC, while amphetamine stereotypy was only slightly increased. No changes in locomotor activity were observed in LC lesioned rats treated with apomorphine and amphetamine. These data indicate that lesions of the LC produce decreased activity of dopaminergic brain neurons as well as supersensitivity of dopaminergic receptors. 48 references. (Author abstract modified)

001394 Kovacs, G. L.; Telegdy, G.; Lissak, K. Department of Pathophysiology, University Medical School, Szeged, Hungary **Correlated effect of corticosterone on hypothalamic serotonin and avoidance behaviour in rats.** Activitas Nervosa Superior (Praha). 19(2):150-152, 1977.

A paper delivered at the Second International CIANS Congress (Prague), concerned with a determination of whether the corticosterone induced change in 5-hydroxytryptamine (5-HT) content is accompanied by some changes of avoidance behavior, is presented. Daily corticosterone treatment of rats resulted in a decreased number of conditioned avoidance reactions during extinction of active avoidance. It is suggested that the concordance of a dose dependent dual effect of corticosterone on hypothalamic 5-HT and behavior indicates that cerebral 5-HT metabolism plays an important role in the behavioral action of corticosterone. 7 references.

001395 Kozlovskaya, Marina M.; Valdman, A. V. Dept. of Pharmacology, Pavlov Medical Institute, Leningrad, USSR **Brain stimulation provoked emotional reactions of cats in a social situation.** Activitas Nervosa Superior (Praha). 19(3):221-222, 1977.

In a paper presented at the second international CIANS congress, a study of provoked emotional reactions in cats induced by brain stimulation and by pharmacologic agents is reported. Weak stimulation of the emotiogenic brain areas in the cat can change its emotional state. Tendency toward leadership or submission, the type of groups formed, initiative, behavior in con-

flict situations and other variables were compared in control and stimulation sessions. Changes in the emotional state inhibited behavioral expressions of positive emotions. The development of changes could be modified pharmacologically. Doxepin removed fear and attacks ceased in one group situation, while Ludiomil eliminated fear and increased aggression and initiative.

001396 Krimmer, Edward C.; Barry, Herbert, III. Department of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15261 **Discriminative pentobarbital effect measured by head movements in restrained rats.** Pharmacologist. 19(2):228, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the discriminative effect of pentobarbital as measured by head movements in restrained rats was reported. The rats were trained to make lateral head movements in opposite directions to obtain water on the basis of the discriminative stimulus attributes of pentobarbital or vehicle. Rapid discriminative learning was indicated by the head turns prior to reinforcement. In tests of 60 sec duration with novel conditions, the ED-50 for pentobarbital was 5.1mg/kg. The response was also elicited by sufficiently high doses of chlordiazepoxide and alcohol. The discriminative stimulus was not based on a general stimulant or depressant effect on response rate, because the drug response was elicited by treatments that increased response rate (pentobarbital) and treatments that decreased response rate pentobarbital, chlordiazepoxide, alcohol compared to saline controls. (Author abstract modified)

001397 Lal, Harbans; Kaplan, Lane; Numan, Robert; Valentino, Dominic. Department of Pharmacology and Toxicology, University of Rhode Island, Kingston, RI 02881 **Acquisition and extinction of operant responding for intravenous injections of fentanyl in the rat.** Communications in Psychopharmacology. 1(3):207-212, 1977.

Acquisition and extinction of operant responding for intravenous injections of fentanyl in the rat was investigated. Lever pressing to obtain fentanyl injections (1microg/kg injection) were achieved in drug naive rats. Within 4 days the daily injection rates reached an average of 429 (S.E.,85). These responses were readily extinguished when the lever pressing failed to activate the injection system. Self-administration was reacquired when availability of fentanyl but not of saline, was again made contingent upon lever pressing. 5 references. (Journal abstract modified)

001398 Lal, Harbans; Valentino, Domenic; Hynes, Martin D. Department of Pharmacology, University of Rhode Island, Kingston, RI 02881 **Differential tolerance to inhibitory action of various neuroleptics on deprivation-stimulated food intake in rats chronically treated with haloperidol.** Pharmacologist. 19(2):174, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of various neuroleptics on deprivation stimulated food intake in rats and on the development of tolerance to this effect after chronic administration of haloperidol was reported. The animals were trained to consume their daily requirement of food in a 2 hr period of food availability and the test drugs were administered intraperitoneally prior to food availability. The dopamine inhibiting neuroleptics haloperidol and benperidol were most active in inhibiting the deprivation induced consumption of food, while the alpha-adrenergic receptor blocking drugs azaperone, chlorpromazine, and phenoxybenzamine were far less active. A marked tolerance to the action of benperidol and haloperidol was observed 7 da to 21 da after discontinuation of chronic haloperidol treatment. Little tolerance was seen to the action of azaperone, chlorpromazine, and phenoxybenzamine. In addition to demonstrating the development of tolerance to the inhibitory action of specific neuroleptics on food consumption, the data suggest a role for dopaminergic mechanisms in feeding behavior stimulated by food deprivation. 1 reference. (Author abstract modified)

001399 Laubie, Michel; Schmitt, Henri; Vincent, Michel; Remond, Georges. I.N.R.S., 14 Rue du Val d'Or, F-92150 Suresnes, France **Central cardiovascular effects of morphinomimetic peptides in dogs.** European Journal of Pharmacology (Amsterdam). 46(1):67-71, 1977.

To determine whether morphinomimetic polypeptides also mimic the cardiovascular effects of morphine like drugs, morphinomimetic peptides were injected into the cisterna magna of chloralosed dogs. Methionine enkephalin was found ineffective but beta-endorphin induced an initial and transient increase in blood pressure and heartrate followed by a delayed hypotension and bradycardia. The synthetic pentapeptides, (d-ala2)met-enkephalin, (d-ala2)met-enkephalinamide also induced a marked hypotensive, bradycardic and sympathoinhibitory effect. High doses of naloxone were required to antagonize these effects transiently. 11 references. (Author abstract modified)

001400 Lee, H. K.; Chai, C. Y.; Wayner, M. J.; Chung, P. M.; Hsu, C. H. Dept. of Biophysics, National Defense Medical Center, P.O. Box 8244, Taipei, Taiwan **Effects of neuroleptics on morphine-induced tail erection in mice.** Pharmacology Biochemistry & Behavior. 7(2):153-157, 1977.

The effects of various drugs on morphine induced tail erection in mice were investigated. Pretreatment with atropine, phenoxybenzamine, propranolol, diphenhydramine, cyproheptadine, or parachlorophenylalanine did not interfere with the dose dependent effects of morphine on tail erection. Several neuroleptic drugs which are dopamine (DA) receptor blocking agents showed a clear antagonistic effect on morphine induced tail erection. Haloperidol and penfluridol blocked morphine induced tail erection at doses which produced only a slight behavioral depression. Pimozide and chlorpromazine were less antagonistic than haloperidol and penfluridol and inhibited morphine induced tail erection only in doses which produced a marked behavioral depression. It is suggested that DA might be involved in tail erection induced by morphine, and that morphine induced tail erection in mice may be a useful model for the evaluation of neuroleptic drugs. 14 references. (Author abstract modified)

001401 Levitt, Robert A.; Baltzer, John H.; Evers, Timothy M.; Stilwell, Donald J.; Furby, John E. Department of Psychology, University of Alabama in Birmingham, Birmingham, AL 35294 **Morphine and shuttle-box self-stimulation in the rat: a model for euphoria.** Psychopharmacology (Berlin). 54(3):307-311, 1977.

In a shuttle box self-stimulation paradigm, analgesic doses of morphine increase the amount of time a rat leaves rewarding brain stimulation on, without altering average off times. This paradigm may serve as a model for the euphoria induced by narcotic drugs and as a useful tool for evaluating the reinforcing effects of drugs. If the rewarding and analgesic effects

of narcotics are inseparable, the psychological dependence resulting from their pleasurable effects may not be preventable without also inhibiting their analgesic action. However, the homeostatic adjustments mediating the physical and psychological dependence resulting from the unpleasantness of drug withdrawal in a dependent individual may still be mediated separately from these other two actions (reward enhancement and analgesia). 27 references. (Author abstract modified)

001402 Lichtblau, Leonard; Fossom, Linda H.; Sparber, Sheldon B. Dept. of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **Beta-endorphin: dose-dependent suppression of fixed-ratio operant behavior.** Life Sciences (Oxford). 21(7):927-932, 1977.

The effects of centrally administered beta-endorphin and morphine on fixed-ratio responding for food reinforcement were examined. Centrally administered beta-endorphin or morphine suppressed fixed-ratio 15, food reinforced responding by rats in a dose dependent manner. Beta-endorphin was 21 times more potent than morphine on a molar basis. Scratching and wet dog shakes were observed within 30 minutes of beta-endorphin administration but were not seen after morphine and did not appear to be responsible for the suppression of the conditioned behavior. 20 references. (Journal abstract)

001403 Liebman, Jeffrey; Segal, David S. CIBA/GEIGY Pharmaceutical Co., Department of Pharmacology, 556 Morris Ave., Summit, NJ 07901 **Differential effects of morphine and D-amphetamine on self-stimulation from closely adjacent regions in rat midbrain.** Brain Research (Amsterdam). 136(1):103-117, 1977.

The effects of morphine were investigated on self-stimulation from numerous electrode placements in the area of the substantia nigra or in the ventral half of mesencephalic central gray matter. Before pharmacological testing, current intensity was reduced to yield stable, submaximal rates of self-stimulation. Rats were then injected daily with morphine for 10 days, and were tested 3 hours after injection. Between days 5 and 10 of treatment, many rats self-stimulated at more than 150% of baseline, but some others reduced self-stimulation to as little as 3% of baseline. Histological evaluation revealed that morphine facilitated self-stimulation when the electrode tip was located more than 0.3mm from substantia nigra or more than 0.2mm from the midline of central gray. In rats with electrode tips closer to substantia nigra or to the midline of central gray, morphine often reduced or failed to alter self-stimulation rates. The effects of a low dose of D-amphetamine were investigated on electrode placements in the substantia nigra area. Placements close to the dorsal border of substantia nigra yielded less facilitation of self-stimulation by D-amphetamine than did placements located more dorsally or medially. Possible catecholaminergic substrates of these differential effects are discussed. 40 references. (Author abstract)

001404 Lindquist, Mats; Andersson, Bengt E.; Gotestam, K. Gunnar. Psychiatric Research Center, University of Uppsala, Uppsala, Sweden **The effect of non-contingent amphetamine injections on the extinction of food- and drug-reinforced lever pressing in rats.** Addictive Behaviors (Oxford). 2(4):167-179, 1977.

To determine the effect of noncontingent amphetamine injections on the extinction of food and drug reinforced lever presssing in rats, male Sprague-Dawley rats thus trained were given noncontingent injections of d-amphetamine (0.25mg/kg), phenmetrazine (1.0or 2.0mg/kg), diethylpropion (1.0mg/kg) or saline prior to self-administration of saline or responding without programmed consequences. Single doses of amphetamine, phenmetrazine, diethylpropion or saline were given before saline was offered for self-administration for 2 or 3 hr in rats previously made dependent on amphetamine. High rate of responding was observed when amphetamine was given before the session. Rats trained in food reinforced lever pressing were given single doses of amphetamine, phenmetrazine or saline before the number of responses without programmed consequences were recorded for 3 hr. Low rate of responding was observed for all pretreatment conditions. A rat trained in food reinforced lever pressing was given a single dose of amphetamine (10mg/kg) each day. Single doses of amphetamine, phenmetrazine or saline were given prior to sessions where the number of responses (without programmed consequences) were recorded for 3 hr. Low rate of responding was observed for all pretreatment conditions. It is concluded that the increased rate of lever pressing for no programmed consequences after single doses of amphetamine is due to the experience of amphetamine during food reinforced behavior, i.e. the drug acts as a discriminative stiumulus for subsequent responding. Also an increased rate of saline self-injections after single doses of an amphetamine analogue can be explained in terms of the drug acting as a discriminative stimulus. It is therefore concluded that the increased rate of responding cannot be explained in terms of a general activity effect of amphetamine or amphetamine analogues. 14 references. (Author abstract modified)

001405 Logue, A. W. 760 William James Hall, Harvard University, Cambridge, MA 02138 **Generalization of the conditioned stimulus in taste aversion.** Research Report, NIMH Grant MH-15494, 1977. 29 p.

Two experiments were performed with rats to investigate stimulus generalization in taste aversion. In Experiment 1, 50 rats were first exposed to .2% saccharin and half of these, the experimentals, then received lithium chloride injections. Controls were injected with distilled water. All rats subsequently had one session with each of five saccharin concentrations, including .2%. In Experiment 2, 15 experimental and 15 control rats were exposed to 2.5% saccahrin for 3 days, followed by injection on the third day. Experimental and control groups then underwent generalization testing for two 5 day periods with 2.5% saccharin and four other concentrations. Both experiments resulted in a marked aversion to all concentrations of saccharin by the lithium chloride animals relative to the controls. Despite numerous procedural differences between the two studies, in both cases generalization gradients passed through a minimum at approximately the concentration which was paired with lithium chloride. The gradients obtained were similar to those found in more traditional learning paradigms. Results indicate that taste aversion may not be a different form of learning with respect to stimulus control. 37 references. (Author abstract)

001406 Lorenzo, A. V.; Gewirtz, Myrna. Children's Hospital Medical Center, Boston, MA 02115 **Effect of d-amphetamine on locomotor activity of lead fed rabbit neonates.** Pharmacologist. 19(2):180, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, in August, 1977, a study of the effect of dextroamphetamine on locomotor activity in 48-day-old rabbits who had been fed 25mg/kg/day of lead acetate from 1 to 30 days of life was reported. No differences in activity were observed between lead fed and nonlead fed littermates. In-

travenous administration of 2mg/kg dextroamphetamine produced slight but detectable increases in the locomotor activity of nonled fed rabbits which lasted about 40 min. In lead exposed animals, dextroamphetamine produced much greater activity that was still increasing after 60 min. The results are consistent with the investigators' previous observation that lead interferes with tryptophan entry into brain and possibly with serotonin synthesis. 2 references. (Author abstract modified)

001407 Lozovskaya, R. G. Lab. srav. onto. vyssh. nerv. deyat., Institut fiziologii im. I. P. Pavlova AN SSSR, Leningrad, USSR **/Effect of chlorpromazine on elaboration and extinction of an instrumental alimentary reflex in puppies./** Vliyaniye aminazina na vyrabotku i ugasheniye instrumental'nogo pishchevogo refleksa u shchenkov. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni I. P. Pavlova (Moskva). 27(1):43-46, 1977.

The role of autonomic adrenoreactive structures in the elaboration and extinction of lever pressing during a food procurement response was studied in 40 - to 50-day-old puppies. A 0.05mg/kg dose of chlorpromazine proved more effective than a 0.5mg/kg dose in reducing both the rate of formation and extinction of the instrumental alimentary reflex. The change in elaboration was connected with appearance at reinforcement anticipation, which is not inherent in normal puppies of an early age. It is assumed that a 0.05mg/kg dose diminishes the adrenergic ascending influences which prevail in normal puppies, while the higher dose exerts both adrenolytic and a cholinolytic action, without changing the balance between the systems or influencing the puppies' behavior. 14 references. (Journal abstract modified)

001408 Maickel, R. P.; Braude, Monique C.; Zabik, J. E. Section on Pharmacology, Medical Sciences Program, Indiana University, Bloomington, IN 47401 **The effects of various narcotic agonists and antagonists on deprivation-induced fluid consumption.** Neuropharmacology (Oxford). 16(12):863-866, 1977.

To examine the effects of narcotic antagonists and agonists on deprivation induced fluid consumption, rats in a standardized deprivation induced fluid consumption test system were given single doses of a variety of narcotic antagonists (cyclazocine, levallorphan, naloxone, or naltrexone) or agonists (meperidine, methadone, morphine, pentazocine, or opium alkaloids). For the narcotic antagonists, dose dependent reductions in fluid intake were obtained, once a threshold level was reached. Subthreshold doses of the antagonists were without effect. In contrast, a variety of narcotic agonists produced biphasic responses, with an initial dipsogenic effect followed by a subsequent dose dependent decrease in fluid consumption as doses were increased. 12 references. (Author abstract modified)

001409 Mailman, R. B.; Krigman, M.; Mushak, P.; Mueller, R. A.; Breese, G. R. University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Lead enhances lithium-induced polydipsia.** Pharmacologist. 19(2):134, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of neonatal lead (Pb) exposure on lithium induced polydipsia was reported. Male Long-Evans rats were intubated with Pb from day 3 through day 30 of life. After 60 days of age, 24 hr water consumption was measured before and after lithium administration to Pb treated rats and to control animals. In control rats, the polydipsic response to lithium was maximal after 7 da of treatment. In Pb treated rats, water consumption was significantly greater than baseline drinking and was greater than the response observed in control animals after lithium administration. Plasma angiotensin I and angiotensin II levels and renin activity were not different between Pb treated and control groups with or without lithium. It is suggested that neonatal Pb exposure alters the responsiveness of the central nervous system to lithium induced polydipsia. This may have relevance to physiological alterations etiologically related to subacute lead exposure. (Author abstract modified)

001410 Maple, P.; Diamond, B.; Havdala, H.; Borison, R. Rush Medical College, Chicago, IL 60612 **Chronic and acutely induced dyskinesias: a pharmacologic distinction.** Pharmacologist. 19(2):154, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of various drugs on stereotyped behavior (SB) induced in rats by acute or chronic administration of dextroamphetamine or phenylethylamine (PEA), an endogenous amphetaminelike stimulant concentrated in the neostriatum and limbic system of human brain, was reported. Haloperidol and pimozide completely blocked all acutely or chronically elicited SB. Clozapine potentiated all acutely induced SB, blocked all chronically PEA induced SB, and had no effect on chronically amphetamine induced SB. The alpha-adrenergic blocker phentolamine affected acutely induced SB in a manner similar to clozapine, while antagonizing all chronically elicited SB. The cholinergic blocker trihexyphenidyl potentiated all amphetamine evoked behaviors but potentiated only acutely induced PEA SB. It is suggested that acutely and chronically induced SB may differ in their pharmacology and that caution should be exercized in extrapolating acute and chronic animal models to chronic progressive neurological disease in humans. (Author abstract modified)

001411 Mares, P.; Kolinova, M.; Fischer, J. Institute of Physiology, Czechoslovak Academy of Sciences, Budejovicka 1083, 14220 Prague 4, Czechoslovakia **The influence of pentobarbital upon a cortical epileptogenic focus in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 226(2):313-323, 1977.

Influence of pentobarbitol on a cortical epileptogenic focus was investigated in the rat. Three subsequent doses of pentobarbital were administered i.p. to 17 rats at 10 minute intervals. Histograms of intervals between individual focal discharges were shifted toward longer intervals even after the smallest dose of pentobarbital: the prolongation of intervals was clearly visible after the third dose in the EEG also. In a primary focus, and especially in a projected mirror focus, the initial positive phase of the focal discharge became more marked after the administration of pentobarbital, while the later component showed a large late negative wave. Development of a large late negative makes the shape of the projected discharge similar to that observed after local application of GABA to a projected focus. Barbiturate spindles present after the first and second dose of pentobarbital were regularly triggered by focal discharges. Results suggest that pentobarbital in anesthetic doses markedly suppresses the activity of a penicillin cortical focus, while smaller doses have a weak antiepileptic effect. 25 references.

001412 Marsh, G.; Linnoila, M. Center for Study of Aging, Duke University, Durham, NC 27710 **Deanol effects on performance and average evoked potentials.** Gerontologist. 17(5, Part I):96, 1977.

In a paper read at the 30th meeting of the Gerontological Society, San Francisco, November 1977, the effects of deanol on performance and average evoked potentials in a reaction time (RT) task were investigated. A RT task with a warning signal was used in which there were eight response keys, any one of which had to be pushed upon illumination. Reduction of the possible response key set to 4 resulted in increased average evoked potentials reflecting increased information load. Treating Ss with 900mg/day deanol for 3 weeks produced larger evoked potentials but no improvement in RT performance. (Journal abstract modified)

001413 Martin, J. R.; Quock, R. M. Department of Physiology and Pharmacology, University of the Pacific, Stockton, CA 95211 **Apomorphine (APO) induced stereotyped behavior, locomotor stimulation and hypothermia in spontaneous hypertensive rats (SHR) and normotensive Wistar rats (NWR).** Pharmacologist. 19(2):155, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the apomorphine induced stereotyped behavior, locomotor stimulation, and hypothermia in spontaneous hypertensive rats (SHR) and normotensive Wistar rats (NWR) was reported. There were no significant differences between SHR and NWR in baseline locomotor activity or rectal temperature. Comparison of accumulated stereotyped behavior scores and locomotor stimulation scores showed no significant differences between the strains. However, apomorphine produced a larger and more prolonged hypothermia in SHR than in NWR. It is suggested that SHR are more sensitive than are NWR to the hypothermic effects, but not to the stereotypic effects or locomotor effects, of apomorphine. (Author abstract modified)

001414 Martindale, Colin; Hines, Dwight. Dept. of Psychology, University of Maine, Orono, ME 04473 **Effects of amphetamine and nembutal on social exploration in the Mongolian gerbil.** Pharmacology Biochemistry & Behavior. 7(6):573-574, 1977.

To determine the effects of amphetamine and nembutal on social exploration in the Mongolian gerbil, male gerbils were injected with one of the drugs or saline and placed in a preference chamber one side of which contained a female gerbil. Amphetamine significantly decreased amount of time in contact with the female. Although the amphetamine effect held for both novel and familiar females, it was more marked for novel than for familiar females. Results are discussed in terms of Eysenck's theory concerning socialization and cortical activation. 9 references. (Author abstract modified)

001415 Matsuzaki, M.; Misra, A. L. New York State Office of Drug Abuse Services, Testing and Research Lab., 80 Hanson Pl., Brooklyn, NY 11217 **Comparison of the convulsant effects of cocaine and pseudococaine in the rhesus monkey.** Brain Research Bulletin. 2(6):417-424, 1977.

The convulsant effects of cocaine and its C2 epimer, pseudococaine on EEg, respiration, heartrate and behavior were studied in the rhesus monkeys with electrodes implanted in the brain. Intravenous injections of cocaine (3.0to 8.0mg/kg) and pseudococaine (3.0to 7.0mg/kg) in the animals produced a similar pattern of clonic convulsions accompanied by marked increases in the heart and respiratory rates with mydriasis and excessive salivation. However, both isomers showed different effects on the EEG and animal's behavior following convulsions; e.g. the cocaine induced convulsions were followed by low voltage fast waves in the EEGs associated with behavioral hyperexcitation, while pseudococaine induced convulsions were followed by high voltage slow waves associated with behavioral depression and drowsiness with intermittent sleep. Pseudococaine was more potent than cocaine in producing convulsions in the same monkeys. The durations of convulsions produced by these drugs were dose dependent. Results are taken to support an earlier suggestion that the limbic system plays an important role in the CNS stimulating and convulsant effects of cocaine and pseudococaine in the monkey, and that the effects of cocaine may be related to the inhibition of electrical activities of the structure of the limbic system. 16 references. (Author abstract modified)

001416 McCarthy, L. E.; Borison, H. L. Dartmouth Medical School, Hanover, NH 03755 **Anti-emetic activity of nabilone, a cannabinol derivative, reversed by naloxone in awake cats.** Pharmacologist. 19(2):230, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of nabilone, a cannabinol derivative, on the emetic effects apomorphine and deslanoside in awake cats was reported. Apomorphine induced vomiting was inhibited by doses of nabilone which produced miminal behavioral disturbance. Complete protection against apomorphine was obtained by doses of nabilone which produced considerable psychomotor impairment. Nabilone was less effective against the emetic effect of deslanoside; vomiting was prevented by doses of the drug which caused severe behavioral disturbance. Naloxone antagonized the antiemetic action of nabilone by temporarily restoring the vomiting response to apomorphine or by precipitating emesis after protection against deslanoside. Tolerance to the behavioral effects of nabilone or to its antiemetic action was not evident with one or two injections per week, allowing complete recovery between tests. (Author abstract modified)

001417 McMillan, D. E.; Leander, J. D. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Effects of chlordiazepoxide on punished and unpunished responding before and during chlordiazepoxide drinking.** Pharmacologist. 19(2):229, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of chlordiazepoxide on punished and unpunished responding in rats before and during chlordiazepoxide drinking was reported. Rats were trained to lever press for food under a multiple fixed-interval schedule where responses during one component were punished with electric shock. A 10mg/kg dose of chlordiazepoxide increased punished responding; 3mg/kg and 30mg/kg of the drug had little effect. The 3mg/kg and 30mg/kg doses of chlordiazepoxide did not affect unpunished responding, but 30mg/kg decreased the rate. The rats were then administered approximately 50mg/kg of chlordiazepoxide daily in drinking water. After 7 weeks of drinking chlordiazepoxide, the rate of punished responding in these rats was about doubled, but unpunished responding was not affected. In rats drinking chlordiazepoxide, injections of the drug increased both punished responding and unpunished responding across a wide range of doses and the increases in rates of punished responding were larger than those observed before chronic administration of the drug. (Author abstract modified)

001418 Meyerson, B.; Berg, M. Institute of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **Influence**

of beta-endorphin on exploratory, social and sexual behaviour in the male rat. Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):64, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the effects of beta-endorphin (END) on exploratory, social, and sexual behavior was studied in castrated male rats maintained on weekly testosterone propionate treatment. Intraventricular injection of END did not influence exploratory activities (ambulations, rearing, sniffing) or social measures (contact, anogenital exploration, amicable or agonistic behavior), but there was a significant decrease of mounting behavior. Self-grooming was increased but not grooming of partner. END treated rats displayed two behaviors not seen in controls; brief periods of immobility (freezing in a certain position) and short bursts of jerky movements. It was concluded that END can specifically influence elements of the rat's normal repertoire of behavior and also induce behavior patterns that are not normally seen.

001419 Miczek, K. A. Carnegie-Mellon University, Pittsburgh, PA 15213 **A behavioral analysis of aggressive behaviors induced and modulated by delta9-tetrahydrocannabinol, pilocarpine, d-amphetamine and L-DOPA.** Activitas Nervosa Superior (Praha). 19(3):224-225, 1977.

In a paper presented at the second international CIANS congress, a study of pharmacologic treatments that induce or initiate aggressive behaviors in Sprague-Dawley rats is reported. Aggressive reactions were induced by delta9-tetrahydrocannabinol, pilocarpine, d-amphetamine, and L-DOPA, and compared to the species specific patterns of fighting generated in pairs of rats in a resident/intruder situation. It is concluded that a large number of drugs can facilitate attack and threat behavior at low dose levels and exert suppressant effects at higher doses. Aggressive responses which are induced or initiated by drug administration are only seen after very high toxic doses or chronic administrations, and differ from the species specific patterns of aggression to consider them as behavioral pathologies.

001420 Miczek, Klaus A. Dept. of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Effects of L-DOPA, d-amphetamine and cocaine on intruder-evoked aggression in rats and mice.** Progress in Neuro-Psychopharmacology. 1(3/4):271-277, 1977.

The effects of L-DOPA, d-amphetamine, and cocaine on previously observed, reliable, intruder evoked aggression in rats and mice were investigated. d-Amphetamine (0.1mg/kg) and L-DOPA (10mg/kg) increased attack behavior in resident rats, but not mice. At higher doses, these drugs and also cocaine reliably suppressed attack without impairing locomotor activity in both species. When L-DOPA and d-amphetamine were administered to the intruder mice and rats, they were attacked more frequently by the undrugged residents. d-Amphetamine and cocaine suppressed attack behavior in mice housed with a female at dose levels four times lower than those required to achieve the same effect in isolated mice. Intruder evoked aggressive behavior is considered an extremely drug sensitive test permitting ready species comparisons that are not possible with other tests of animal aggression. 23 references. (Author abstract)

001421 Miliaressis, Eleftherios. Faculte de Psychologiiee, Universite d'Ottawa, 1245 Kilborn, Ottawa K1H 6K9, Canada **Serotonergic basis of reward in median raphe of the rat.** Pharmacology Biochemistry & Behavior. 7(2):177-180, 1977.

The involvement of serotonergic neuronal mechanisms in the mediation of self-stimulation in the median raphe (MR) was investigated in rats. The animals were trained to self-stimulate simultaneously in the ventromedian tegmentum (VMT) and the MR by pressing two independent bars. Bar-pressing rates for VMT self-stimulation were increased following methamphetamine and decreased following alpha-methyl-paratyrosine, while MR self-stimulation was not significantly affected. MR self-stimulation was specifically decreased following para-chlorophenylalanine. These results support the hypothesis that self-stimulation in the MR is due to the stimulation of serotonergic neuronal elements. The data also indicate that self-stimulation of neither the VMT nor the MR is dependent upon intact neurotransmitter mechanisms in the other structure, suggesting that the two reward systems are relatively independent. 9 references. (Author abstract modified)

001422 Mogilnicka, E.; Klimek, V. Institute of Pharmacology, Polish Academy of Sciences, 31-343 Cracow, Poland **Drugs affecting dopamine neurons and yawning behavior.** Pharmacology Biochemistry and Behavior. 7(4):303-305, 1977.

The effects of different dopamine (DA) agonists and antagonists on DA neurons and yawning behavior were investigated in the rat. Drugs stimulating the DA neurons in different ways and given in low doses induced yawning in rats. These drugs included apomorphine, piribedil, amphetamine, nomifensine, and L-dopa. Blockade of DA receptors with neuroleptics counteracted DA agonists induced yawning. It is concluded that this action may indicate a dopaminergic component of this behavior. 11 references. (Author abstract modified)

001423 Murray, Thomas F.; Horita, Akira. University of Washington School of Medicine, Seattle, WA 98195 **Effects of phencyclidine on operant behavior in rats.** Pharmacologist. 19(2):228, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of phencyclidine on operant behavior in rats trained to respond on a variable interval schedule of water reinforcement was reported. Intraperitoneal phencyclidine significantly increased response rates in a dose dependent manner. Higher doses reduced response rates and very high doses almost abolished responding. This biphasic effect of phencyclidine is qualitatively similar to that observed with amphetamine. Other groups of rats received daily treatments of phencyclidine immediately prior to or immediately after the operant session. When animals in both groups were treated prior to the operant session on a test day, they displayed complete tolerance to the rate depressant effect of phencyclidine. It is posited that the observed tolerance to the drug is not dependent on behavioral compensatory mechanisms. (Author abstract modified)

001424 Myers, Richard H.; De Castro, John M. Department of Psychology, Georgia State University, University Plaza, Atlanta, GA 30303 **Learned aversions to intracerebral carbachol.** Physiology & Behavior. 19(4):467-472, 1977.

To test the generality of proposed intracerebral carbachol induced debilitation, the learned taste aversion paradigm was used to assess the effects of microinjections of the compound to the rat medial septum, lateral ventricle, and ventral hippocampus. Either a central cholinergic blocker (atropine sulfate) or a peripheral cholinergic blocker (atropine methyl nitrate) was administered concomitantly with carbachol to determine the locus of action. Carbachol administered to the

medial septum resulted in a learned taste aversion that was mediated by central cholinergic systems. Administrations to the lateral ventricle resulted in the same aversion mediated by a peripheral cholinergic effect. Administrations to the ventral hippocampus did not cause a learned taste aversion, but conditioned an aversion to being handled. It is concluded that centrally administered carbachol produces an altered internal state which is aversive to the animal, and the mechanism underlying this phenomenon is dependent upon administration site. 30 references. (Author abstract modified)

001425 Noguchi, Setsuko; Iwahara, Shinkuro. Mitsubishi-Kasei Institute of Life Science, 11 Minamiooya, Machida-shi, Tokyo 194, Japan **Effects of magnesium pemoline on pattern discrimination learning in young rats.** Psychologia (Kyoto). 20(3):159-162, 1977.

The effects of magnesium pemoline (MgPe) a central stimulant, on pattern discrimination learning in young rats was investigated. Starting on the 7th day from birth, rats were given orally 0.1to 0.2ml per day of carboxymethylcellulose solution with or without MgPe. From the 28th day or the 41st day, the rats were trained on a pattern discrimination task, motivated by electric shock. At the same time, the drug rats were given 20mg/lml/kg of MgPe, and the control rats were similarly treated with the same volume of the solution without having received the drug prior to the daily session. Results indicated a significant facilitative effect of MgPe on pattern discrimination even when training started at the 28th or the 41st day. The drug rats ran significantly faster than the control rats but this time measure was not correlated with the learning measure. MgPe was also shown to facilitate reversal learning but failed to affect the retention of the original discrimination, possibly due to the ceiling effect. 6 references. (Author abstract)

001426 Norton, Stata. Dept. of Pharmacology, Coll. of Health Sciences and Hospital, University of Kansas Medical Ctr., Kansas City, KS 66103 **The structure of behavior of rats during morphine-induced hyperactivity.** Communications in Psychopharmacology. 1(4):333-341, 1977.

The structure of behavior and motor activity of rats under morphine induced hyperactivity was investigated. Rats receiving morphine sulfate, 1 or 2 mg/kg s.c.,show changes in frequency of behavioral acts which are compatible with other reports that low doses of morphine cause hyperactivity in rats. Standing and looking are decreased, while walking, rearing, turning, sitting and grooming are increased. The linkage of behavior acts as behavior patterns is not significantly affected by morphine when measured by correlation with behavior patterns after saline. However, all behaviors, except standing, become more random in their distribution after morphine. Previous studies have shown that amphetamine also has effects on the structure of behavior but the primary effects of the two drugs on the structure of behavior differs at doses of both drugs which cause hyperactivity. 7 references. (Author abstract modified)

001427 Novack, Gary Dean. University of California, Davis, CA **Benzhydryl piperazines: a neuropharmacological and psychopharmacological evaluation. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-27400 HC$15.00 MF$8.50 150 p.

The neuropharmacological and psychopharmacological effects of three benzhydryl piperazines -- SC-13504 (an anticonvulsant), hydroxyzine (HDX, an anxiolytic), and chlorcyclizine (CCZ, an antihistaminic) -- were evaluated. SC-13504 was a more effective anticonvulsant than either HDX or CCZ in maximal electroshock seizures in rats and pentylenetetrazol induced seizures in mice. None elicited drug discrimination in rats in an active avoidance, T-maze paradigm; nor did any drug elicit state dependent learning in mice in a passive avoidance, one trial learning paradigm. HDX and CCZ blocked conditioned avoidance responses at doses that did not abolish escape. In rats, high CCZ and HDX doses elicited severe clonic seizures and death. In mice, CCZ and HDX elicited ataxia and sedation, and moderate doses of SC-13504 induced a cataleptic state and death. It is concluded that, although all three benzhydryl piperazines are similar in effects, SC-13504 is a more selective anticonvulsant than HDX or CCZ. (Journal abstract modified)

001428 O'Connor, M. F.; Piepho, R. W.; Ryan, C. F. Nebraska Medical Center, College of Pharmacy, Omaha, NE 68105 **Physical dependence associated with chronic methaqualone administration.** Pharmacologist. 19(2):231, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study in which the dependence producing liability of methaqualone was compared with that of phenobarbital was reported. Three groups of rats received increasing doses of methaqualone or phenobarbital via the diet, or a control diet. Intoxication and withdrawal symptom scores were determined, and revealed that the methaqualone treated animals experienced a more rapid loss of intoxication and a quicker onset and shorter duration of withdrawal symptoms than did the phenobarbital treated animals. Administration of the drug treated diets led to lower body weights prior to withdrawal. At the end of the withdrawal phase, the methaqualone treated rats had gained more weight than the control or phenobarbital dependent animals. The methaqualone abstinent rats also exhibited increased activity during the drug free period when compared to control. The data indicate that physical dependence on methaqualone can be demonstrated in animals and that the resultant withdrawal syndrome is associated with significant mortality. (Author abstract modified)

001429 Ogren, Sven-Ove; Ross, Svante B. Research and Development Laboratories, Astra Lakemedel AB, S-15185 Sodertalje, Sweden **Substituted amphetamine derivatives. II. Behavioural effects in mice related to monoaminergic neurones.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(4):353-368, 1977.

To further elucidate behavioral effects related to monoaminergic neurones of substituted amphetamine derivatives, the effects of tor-amphetamine (A), 2-, 3- and 4-chloroamphetamine (CA), 4-methylamphetamine (MA) and chlorphentermine (CP) in producing central stimulation (increase in motor activity), antagonism of the reserpine syndrome, potentiation of L-DOPA and 5-hydroxytryptophan (5-HTP) responses in mice were investigated. The inhibitors of the membrane amine uptake desipramine (DMI) and chlorimipramine (CI) were also included in the study. It was found that A had the greatest central stimulating potency, with CP showing least potency. 2-CA, DMI, and CI decreased the motor activity. The decrease in motor activity (sedation) produced by reserpine was only reversed by A, 3-CA, and 2-CA. Alpha-methyltyrosine but not para-cholorophenylalanine, antagonized the reversal effect. Three of the compounds (3-CA, 4-CA, and MA) produced head twitches in the reserpinized mice. The 5-HTP syndrome was potentiated most by MA with 3-CA showing the least abservable effect, whereas A, 2-CA, and DMI had no effect. 37 references. (Author abstract modified)

001430 Ohman, R.; Larsson, M.; Nilsson, I. M.; Engel, J.; Carlsson, A. Dept. of Psychiatry III, Lillhagens Hospital, S-42203 Hisings Backa 3, Sweden **Neurometabolic and behavioural effects of haloperidol in relation to drug levels in serum and brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 299(2):105-114, 1977.

A modified gas chromatographic method for the determination of nanogram quantities of haloperidol, an antipsychotic drug, in serum and discrete brain tissues is described. The procedure was used to investigate tissue distribution and elimination of haloperidol and correlations between drug concentrations in serum and brain and the neurometabolic and behavioral effects of the drug in the rat. No strict correlation was found between serum and brain concentrations of haloperidol; after acute and chronic administration, there appeared to be a saturating dose above which the brain concentration of the drug increased very little. The dose coincided with the dose beyond which little increase in dopa formation occurred. Pharmacokinetic analysis suggested an element of saturable binding or transfer of haloperidol to brain tissue. This mechanism was not preferentially localized to areas of brain rich in dopaminergic synapses. The elimination of haloperidol from brain tissue was multiphasic, with the fourth phase of elimination being the slowest (half-life 4 days). Good correlation was found between haloperidol concentration in the brain and the drug's effects on conditioned avoidance, on serum prolactin values, and on brain dopa formation. 37 references. (Author abstract modified)

001431 Osborne, Steve R.; Rysberg, Jane; Killeen, Peter. Department of Psychology, Arizona State University, Tempe, AZ 85281 **The effects of scopolamine on the temporal control of behavior.** Physiology & Behavior. 19(1):79-85, 1977.

The effects of scopolamine on temporal control of behavior were studied in White Carneaux pigeons. Pigeons were provided access to food once every 75 sec independently of their behavior. The effects of scopolamine hydrobromide on the temporal distribution of locomotor activity during the interfood interval were evaluated on the basis of the model developed by Killeen. Drug induced changes in activity showed the scopolamine: 1) decreased the effect of postfood inhibition; 2) decreased the effect of terminal behaviors that occur late in the interfood interval and compete or interfere with general activity; 3) decreased the total amount of the activity engendered by the appetitive schedule of reinforcement; and 4) appeared to produce an underestimation of time intervals. 29 references. (Author abstract modified)

001432 Pelham, Russell W.; Lippa, Arnold S.; Sano, Mary C. Cardiovascular-Central Nervous System Research Section, Lederle Labs., Pearl River, NY 10965 **Effects of 6-hydroxydopamine on body weight: feeding deficits or sensory-motor impairments?** Communications in Psychopharmacology. 1(6):553-563, 1977.

Experiments were conducted to study the contribution of sensorimotor factors to the development of feeding and drinking deficits following 6-hydroxydopamine and pargyline treatment in rats. Increasing the accessibility of food and water prevented the aphagia and adipsia following intraventricular 6-hydroxydopamine and parenteral pargyline. This drug treatment also delayed eating in response to 2-deoxy-D-glucose and increased the neurological deficits observed after 2-deoxy-D-glucose or alpha-methyl-para-tyrosine. The results suggest that sensorimotor deficits may account for some of the behavioral disturbances observed with 6-hydroxydopamine. 40 references. (Author abstract modified)

001433 Pert, Agu; DeWald, Louise A.; Liao, Helen; Sivit, Carlos. Clinical Center, Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Effects of opiates and opioid peptides on motor behaviors: sites and mechanisms of action. (Unpublished paper).** Bethesda, MD, NIMH, 1978. 33 p.

A series of experiments was undertaken to examine the mechanisms and sites of action of opiate alkaloids and opioid peptides in modulation of motor behaviors. Morphine sulphate, beta-endorphin, or D-Ala2-met-enkephalide (D-Ala) i.v. all produced an initial depression in locomotor activity which was followed by motor excitation. No qualitative differences were noted in the actions of these three compounds. Intracerebral (ic) injections of morphine or D-Ala into the nucleus accumbens produced a gradual increase in activity, while apomorphine produced an immediate increase in spontaneous activity. Morphine induced hyperactivity was antagonized by naloxone but not by haloperidol, while apomorphine activity was antagonized by haloperidol but not by naloxone. Morphine, beta-endorphin, or D-Ala produced significant catatonic reactions characterized by muscular rigidity. Of interest is the decrease in vertical activity and increase in horizontal activity and lateral head movement following morphine injection into the substantia nigra. A rotational model was used to further examine opiate effects on the nigrostriatal system in 6-hydroxydopamine lesioned animals. It was found that opiates clearly increased the activity of the ascending dopaminergic nigrostriatal system and chronic morphine administration produced a progressively greater response. 49 references.

001434 Pickworth, W. B.; Sharpe, L. G.; Nozaki, M.; Martin, W. R. NIDA, Division of Research, Addiction Research Center, Lexington, KY 40583 **Sleep suppression induced by intravenous and intraventricular infusions of methoxamine in the dog.** Experimental Neurology. 57(3):999-1011, 1977.

To examine the effects of methoxamine, a long-acting direct alpha-adrenergic agonist, on sleep, cortical and hippocampal electroencephalograms, nuchal electromyograms, and electrooculograms were recorded from beagle type dogs in an isolation chamber while their behavior was observed on a videomonitor. Following intravenous saline, total sleep occurred during roughly 61% of the 2 hr recording period. Of that time, about 35% were in light sleep, 54% in slow wave sleep, and 11% in paradoxical sleep. An intravenous dose of 0.33mg/kg methoxamine caused no significant changes, whereas a 0.66mg/kg dose significantly reduced total sleep and paradoxical sleep. When infused into the dorsal aspect of the third ventricle, methoxamine (100, 400 or 1200 micrograms) produced no significant effects. However, these doses of methoxamine injected into the ventral third ventricle caused a significant dose related decrease in total sleep, slow wave sleep, and paradoxical sleep and an increase in light sleep. Phenoxybenzamine (4mg/kg, intravenously) pretreatment significantly antagonized the arousal effects of methoxamine administered into the ventral third ventricle. The distribution of infusions of a contrast medium amd bromphenol blue into the dorsal and ventral third ventricle differed in that infusions at the former site did not reach anterior hypothalamic structures. In other experiments, tritium labeled methoxamine was found to cross the blood-brain barrier in the rat. These results suggest that methoxamine is a centrally active alpha-adrenergic agonist and support the concept that hypothalamic adrenergic mechanisms are involved in electroencephalographic and behavioral arousal. 33 references. (Author abstract modified)

001435 Plevova, J.; Formanek, J.; Holoubkova, E.; Tikal, K. Dept. of Pharmacology, Medical Faculty of Hygiene, Srobarova 50, Praha-Vinohrady, Czechoslovakia **An attempt to predict the duration of pentobarbital narcosis on the basis of exploratory activity, defecation rate and body weight of rats.** Activitas Nervosa Superior (Praha). 19(3):176-177, 1977.

The dependence of pentobarbital narcosis duration on some features of innate behavior in rats was investigated. Vertical and horizontal exploratory activity, frequency of defecation, and bodyweight in 74 adult Wistar rats were determined and used as independent variables, while the individual duration of narcosis in these same animals following an injection of 30mg/kg pentobarbital sodium served as the dependent variable. Although some correlation was found between individual and mean values for some independent variables and the mean effect of the dependent variable, the number of secondary random influences bearing on the physiological function and pharmacological effect may be so numerous that the correlation determined is not applicable for predicting the duration of narcosis.

001436 Pryor, G. T.; Larsen, F. F.; Carr, J. D. SRI International, Menlo Park, CA 94025 **Interactions of delta9-tetrahydrocannabinol with phenobarbital, ethanol and chlordiazepoxide.** Pharmacology Biochemistry and Behavior. 7(4):331-345, 1977.

The acute, reciprocal dose response interactions between delta9-tetrahydrocannabinol (delta9-THC) and each of three depressants, phenobarbital (PB), ethanol (ETOH), and chlordiazepoxide (CDP), were studied in the rat for their effects on performance of a conditioned avoidance response (CAR), photocell activity, heartrate, body temperature, and rotarod performance. Delta9-THC impaired CAR and rotarod performance, depressed photocell activity, and decreased heartrate and body temperature. None of the three depressants significantly influenced CAR performance but they all decreased photocell activity and impaired rotarod performance at one or more doses. PB and ETOH also decreased heartrate and body temperature at the highest doses. When combined with each of the three drugs at some dose combinations caused greater depressant effects on most measures than were caused by either drug alone. Only CDP did not augment the impairment of CAR performance caused by the delta9-THC. The highest dose combinations of delta9-THC and each of the three drugs almost completely eliminated photocell activity and rotarod performance. The interactions were also studied after subacute treatment for six days with delta9-THC and/or each of the three depressants. There was clear evidence for tolerance to the effects of delta9-THC on all measures and this tolerance generally resulted in less interactive effects between delta9-THC and each of the depressants. There was also evidence for tolerance to the effects of PB and ETOH on some measures but not CDP. The reduction of effects alone or combined with delta9-THC could be accounted for by assuming a partial loss of potency after subacute treatment that decreased the pharmacologically effective doses of either or both interacting drugs. 41 references. (Author abstract modified)

001437 Quattrone, A.; Bendotti, C.; Recchia, M.; Samanin, R. Clinica Neurologica, Universita di Napoli, Napoli, Italy **Various effects of d-amphetamine in rats with selective lesions of brain noradrenaline-containing neurons or treated with penfluridol.** Communications in Psychopharmacology. 1(6):525-531, 1977.

Various effects of d-amphetamine such as anorexia, increase of locomotor activity and stereotyped behavior were studied in rats with electrolytic lesions of the ventral noradrenergic bundle (VNB) or locus coeruleus (LC) or treated with penfluridol. The anorectic effect of 1.25mg/kg i.p. of d-amphetamine was completely prevented by VNB lesions but not by lesions in the LC or treatment with penfluridol. Conversely, the effect of a higher dose, 2.5mg/kg, was partially reduced by penfluridol pretreatment but not by VNB or LC lesions. Penfluridol completely blocked the increase of locomotor activity and stereotyped behavior induced by d-amphetamine while VNB and LC lesions had no effect. These findings indicate that the anorectic effect of a low dose of d-amphetamine can be dissociated from the effects on motor behavior as regards the involvement of brain catecholamines in the activity of this drug. 17 references. (Author abstract)

001438 Quinton, Elton E.; Bloom, Alan S. Dept. of Psychology, University of Louisville, Louisville, KY 40208 **Effects of d-amphetamine and strychnine on cycloheximide -- and diethyldithiocarbamate-induced amnesia in mice.** Journal of Comparative and Physiological Psychology. 91(6):1390-1397, 1977.

To determine whether immediate posttraining or pretest administration of the adrenergic stimulant d-amphetamine (d-amp) could affect cyclohexamide (CYC) or diethyldithiocarbamate (DDC) induced amnesia in an experimental paradigm that has not produced any evidence of spontaneous recovery of memory, groups of male C57BL/6J mice were administered CYC or DDC 30 min before or immediately after training on a passive avoidance task and tested 72 hr later. Some CYC pretreated groups were given strychnine or d-amp immediately after training and others were given d-amp 1 hr after training. Some DDC pretreated groups were given d-amp or strychnine as described above for CYC groups. Immediate posttraining administration of 5mg/kg d-amp, but not strychnine prevented amnesia in CYC pretreated mice. The DDC induced an apparent amnesia when administered from 30 min before training to 3 hr after training. Posttraining administration of d-amp or strychnine did not prevent DDC induced amnesia. These results are discussed in relation to previous suggestions that CYC and DDC induced amnesia may be the result of a functional impairment of catecholamine neurotransmitter systems by these drugs. 22 references. (Author abstract modified)

001439 Rachid, Cynthia; de Souza, Ademar S.; Izquierdo, Ivan. Disciplina de Neurofisiologia, Dept. de Biofisica, Escola Paulista de Medicina, Rua Botucatu 862, 04023 Sao Paulo, SP, Brazil **Effect of pre- and post-trial tyramine and guanethidine injections on an appetitive task in rats.** Behavioral Biology. 21(2):294-299, 1977.

The effect of tyramine and of guanethidine on bar-pressing for water in rats was investigated. The drugs were injected before (experiment 1) or 1 min after (experiment 2) each daily session. In experiment 1, tyramine had no effect on the number of shaping sessions to criterion (six consecutive bar-presses), on the number of rewarded responses during shaping, or on the number of bar-presses during continuous reinforcement (CRF). Pretrial guanethidine caused a slight increase of the mean number of shaping sessions to criterion. In experiment 2, tyramine caused a reduction of the number of shaping sessions and an increase of rewarded responses both during shaping and during CRF, whereas guanethidine had opposite effects on the three variables. 18 references. (Author abstract modified)

001440 Radulovacki, M.; Buckingham, R. L.; Chen, E. H.; Kovacevic, R. Department of Pharmacology, University of ILlinois Medical Center, Chicago, IL 60612 **Similar effects of**

tryptophan and sleep on cisternal cerebrospinal fluid 5-hydroxyindoleacetic and homovanillic acids in cats. Brain Research (Amsterdam). 129(2):371-374, 1977.

To determine whether chemical changes in cerebrospinal fluid (CSF) produced by tryptophan parallel those occurring during natural slow wave sleep (SWS), data for CSF, 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA) were obtained and SWS was monitored by EEG following placebo or L-tryptophan administration to cats. Analysis of data obtained during wakefulness, SWS, after placebo, and after tryptophan indicated no significant difference in mean HVA levels, while mean 5-HIAA levels differed significantly in the four conditions. Results indicate similar effects of L-tryptophan and SWS on the levels of 5-HIAA and HVA in cisternal CSF, and suggest increased metabolism of 5-hydroxytryptamine (5-HT) in both cases. It is suggested that the crucial factor in the induction of physiological sleep may be the availability of increased amounts of trytophan in the brain at times when sleep mechanisms are ordinarily triggered. 15 references.

001441 Rao, T. R. University of Mysore, Mysore, India **Effect of Curcumen longa on emotionality and learning.** Indian Psychological Review (Agra). 15(1):13-16, 1977.

The effects of Curcumen longa (turmeric), a widely used spice, on emotionality and learning was studied in rats. The Ss, 35 male and 30 female albino rats of Wistar strain, were fed for 50 days with 1 to 6% Curcume longa by mixing the drug with laboratory feed. The emotionality scores and learning scores were measured using a randomized block design. The results indicated an increased rate of change in bodyweight in male rats. After feeding for 21 days, a marked change in bodyweight of all the Ss was observed. Although a significant difference was not found in the defecation scores, a significance was found in the ambulation scores. A tendency indicating an inverse relationship at 1 and 2% levels and a linear relationship at other levels was observed so far as learning scores were concerned. Sex differences in learning also varied depending on the level of treatment. 2 references. (Author abstract modified)

001442 Rech, R. H.; Commissaris, R.; Ford, R. D.; Braude, M. C. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Tolerance and cross-tolerance to CNS depressants after chronic pentobarbital.** Pharmacologist. 19(2):231, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the development of tolerance and cross-tolerance to CNS depressants after chronic pentobarbital in rats was reported. Pentobarbital was administered in food to rats trained to walk the rotarod. After 2 da of chronic pentobarbital, the rotarod disruption from a test dose of pentobarbital was reduced in duration. After 3 to 4 weeks of chronic administration, this test dose no longer impaired rotarod performance. Rats then removed from the diet showed no obvious withdrawal signs and regained their original sensitivity to ip pentobarbital by 2.5weeks. In rats maintained on chronic pentobarbital, ethanol impaired rotarod performance more than in controls. When chronic pentobarbital was removed 8 to 12 hr before the ethanol test, rotarod performance was somewhat less impaired in chronic subjects than in controls. Chronic pentobarbital animals withdrawn for 12 hr prior to testing showed much less rotarod disruption after diazepam or methaqualone than did controls. Controls tested repeatedly with pentobarbital or ethanol showed behavioral tolerance, but this was moderate as compared to the level of tolerance developed by chronic pentobarbital treated animals. It is concluded that complex patterns of cross-tolerance to CNS depressants develop in rats. (Author abstract modified)

001443 Reicher, Murray A.; Holman, Eric W. UCLA, Los Angeles, CA 90024 **Location preference and flavor aversion reinforced by amphetamine in rats.** Animal Learning & Behavior. 5(4):343-346, 1977.

To associate the identical drug state with both a location and a flavor, rats were given intraperitoneal amphetamine injections and then confined for 20 min in one side of a shuttlebox with access to a flavored solution; on control trials without injections, they were confined for 20 min in the opposite side with a different flavor. In the first experiment, the rats were placed in the shuttlebox immediately after injections. In the second experiment, they were placed in the shuttlebox 20 min after injections. In subsequent free choice tests in both experiments an increased choice of the side of the shuttlebox associated with amphetamine is revealed as well as an aversion to the flavored solution associated with the drug. 5 references. (Author abstract)

001444 Rosecrans, John A.; Krynock, Glenn M. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **A possible role of the PAG in the mediation of subjective effects of morphine.** Pharmacologist. 19(2):171, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the involvement of the periaqueductal (PAG) area in the mediation of morphine induced subjective effects in the rat was reported. Rats were trained to discriminate morphine sulfate (MS) from saline using a two bar operant procedure. After learning, cannulae were unilaterally implanted into the PAG. Injection of MS into the PAG produced stimulus control similar to that occurring following systemic MS. The highest dose of MS elicited MS correct responding significantly more than did either systemic or intracerebral saline, and did not differ from systemically administered MS. Injection of naloxone into the PAG effectively blocked the discriminative cue of systemic MS. It is suggested that the discriminative stimulus effects of MS may be mediated by the PAG, which has previously been implicated in the mediation of morphine induced analgesia, tolerance, and physical dependence. (Author abstract modified)

001445 Rosen, Ellen F.; Westlake, Kathleen C.; Petty, Linda C. College of William and Mary, Williamsburg, VA 23185 **The effects of hormones and morphine on both analgesia and the lordosis response produced by cervical probing in the female rat.** Physiological Psychology. 5(3):315-320, 1977.

Two experiments were conducted to assess the effects of sex hormones and morphine on the lordosis response and the analgesia produced by cervical probing in the female rat. Estrogen and progesterone were found not to affect responses to standard tests of nociception (tail flick and tail pressure), but estrogen did increase the lordosis response. Cervical probing and morphine were both found to produce significant analgesia, but hormones did not alter the effectiveness of either. Thus, the pain blocking mechanism involved is apparently not hormone dependent. 21 references. (Author abstract)

001446 Rowland, Neil; Engle, David J. Dept. of Psychology, University of Pittsburgh, Pittsburgh, PA 15260 **Feeding and drinking interactions after acute butyrophenone administration.** Pharmacology Biochemistry and Behavior. 7(4):295-301, 1977.

The effects on feeding and drinking in rats of various doses of droperidol, haloperidol and spiroperidol were studied in a number of paradigms. All three butyrophenones produced generally similar effects. After food deprivation, feeding was slightly increased at low doses but was decreased at the higher doses; the concomitant postprandial drinking was attenuated at all doses. Desalivate rats showed a marked attenuation of feeding (and prandial drinking) at low doses, but when wet mash was given instead of pellets and water a normal dose response relationship was obtained. After water deprivation drinking was attenuated at all doses, and when food was also available during the drinking test the food intake was decreased in proportion to the drinking. Drinking was blocked more when food was present than in its absence. Insulin and 2-deoxyglucose induced feeding in sated rats was attenuated but not abolished by haloperidol. The findings are discussed relative to the role of activation and brain catecholamines in feeding and drinking. 25 references. (Autl.or abstract)

001447 Roy, Edward James. University of Massachusetts **Effects of antiestrogens on eating, female sexual behavior, and the uptake of 3H-estradiol in the central nervous system in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-15114 HC$15.00 MF$8.0 110 p.

To assess the inhibitory behavioral actions of antiestrogens, the hypothesis that antiestrogens compete with estradiol for binding sites in the brain was tested in rats, and the effects of these compounds on estradiol binding were compared with effects on female sexual behavior. The nonsteroidal antiestrogens, MER-25, CI-628 and nafoxidine reduced the uptake of 3H-estradiol in whole homogenates, isolated cell nuclei of brain tissues, and in similar paradigms blocked induction of female sexual behavior. The antiestrogens were injected intraperitoneally 2 hours prior to an intravenous injection of 3H-estradiol, and Ss were killed 2 hours after the latter injection. Results indicated that the antiestrogens can prevent or reverse the nuclear concentration of estradiol in brain cells and were consistent with a postulated role of the cell nucleus in the induction of estrous behavior by estradiol. (Journal abstract modified)

001448 Rudy, Jerry W.; Cheatle, Martin D. Department of Psychology, Princeton University, Princeton, NJ 08540 **Odor-aversion learning in neonatal rats.** Science. 198(4319):845-846, 1977.

To study changes in learning capabilities and identify neurological and neurochemical changes of functional significance to the learning process of the rat, 2-day-old rats were exposed to a novel odor and injected with an illness inducing drug, lithium chloride. When tested at 8 days of age, these pups avoided pine shavings scented with the odor, whereas control pups did not. These results are seen to imply that rat pups are capable of associative learning at a much earlier age than was thought possible. 8 references. (Journal abstract)

001449 Rusterholz, D. B.; Spratt, J. L.; Long, J. P.; Barfknecht, C. F. Dept. of Pharmacolcgy, College of Medicine, University of Iowa, Iowa City, IA 52242 **Evaluation of substituted-amphetamine hallucinogens using the cat limb flick model.** Communications in Psychopharmacology. 1(6):589-592, 1977.

The cat limb flick model was used to evaluate several substituted amphetamine hallucinogens. Intraperitoneal administration of 0.1mg/kg of DOM(STP) or R-(-)-DOB, or 1.0mg/kg of 2,5-DMA produced a significant increase in the number of limb flicks that occurred during a 1 hour observation period. S-(+)-DOB and DOET (0.1mg/kg i.p.)increased the number of flicks observed but not significantly at the sample size and dose used. The alpha-ethyl analog of DOM, BL3912A, produced almost no increase in flick responding. Results are taken to confirm the usefulness of the model for studying hallucinogens of the amphetamine type. 9 references. (Author abstract)

001450 Sackler, A. M.; Weltman, A. S.; Johnson, L.; Tsai, P. Laboratories of Therapeutic Research, Brooklyn College of Pharmacy, L.I.U., Brooklyn, NY 11216 **Effects of methylphenidate (M) on activity of whirler mice (W).** Pharmacologist. 19(2):174, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of orally administered methylphenidate, which has been used to treat hyperactive children, on the circling activity of male whirler mice was reported. A single daily dose of 1mg/kg/day was initially given but the frequency and dosage were increased by the fourth week. The first dose of methylphenidate caused an insignificant increase in circling. By the fourth week, the control group showed significant increases in circling activity. Despite increasing doses of methylphenidate, decreases in activity in the test group were noted at the second, fourth, and eighth weeks. At the eighth week, significant numbers of test mice were found to have decreased circling activity. It is suggested that the circling (or waltzing) activity of these mutant mice may be useful as an animal model for hyperactivity and minimal brain damage studies. (Author abstract modified)

001451 Saito, Hiroshi; Tsuchiya, Moriyoshi; Naka, Shinichi; Takagi, Keijiro. University of Tokyo, Bunkyo-ku, Tokyo 113, Japan **Effect of panax ginseng root on conditioned avoidance response in rats.** Japanese Journal of Pharmacology (Kyoto). 27(4):509-516, 1977.

Pole climbing and shuttlebox tests were employed to study conditioned avoidance response (CAR) and discrimination behavior in rats given extracts from Panax Ginseng root intraperitonealy. Neutral saponins (GNS), a water soluble fraction (GF4) which does not contain saponins, and a lipid soluble fraction (GNo. 5) inhibited CAR and discrimination ability between 500 Hz sound with electric shock (SP) and 1000 Hz sound without shock (S delta). Small doses of GNo.5and ginsenoside Rg fraction (GRg) produced a slight shortening of the response latency (RL) to the conditioned stimulus in CAR. GNo.5produced the incorrect response to S delta. Significant changes in the extinction of CAR were not evident with any fraction. Data from these tests indicate that Panax Ginseng root contains at least three sedative compounds. 9 references. (Author abstract)

001452 Sanchez-Ramos, J. R.; Schuster, Charles R. Dept. of Pharm. and Phys. Sciences, University of Chicago, Pritzker School of Medicine, 950 East 59th Street, Chicago, IL 60637 **Second-order schedules of intravenous drug self-administration in rhesus monkeys.** Pharmacology Biochemistry and Behavior. 7(5):443-450, 1977.

To examine the reinforcing effects of morphine apart from its other pharmacological effects and to determine the morphine/naloxone dose ratio necessary for extinction of self-administration behavior, lever-pressing behavior was generated and maintained in three rhesus monkeys by intravenous infusions of morphine or cocaine under a second order schedule of reinforcement. Under this schedule, every 10th lever press

response (FR-10) during a fixed-interval of time produced a 2 sec stimulus light. The first FR-10 completed after a 60 min interval had elapsed produced the stimulus light and an intravenous infusion of morphine or cocaine. The stimulus light remained on for the duration of the drug infusion (50 to 60 sec). Sessions of morphine or cocaine presentation, each with distinct stimulus light conditions, alternated on a daily basis. Under this schedule, single doses of morphine from 0.125 to 1.0mg/kg maintained high overall response rates (maximum of 40 Rs/min) in the pattern characteristic of fixed-interval schedules of reinforcement. There was no functional relationship between the response rates and the doses of morphine tested. The simultaneous infusion of naloxone (0.125mg/kg) with morphine (0.25mg/kg) markedly decreased response rates. However, the infusion of the same dose of naloxone 5 min after the presentation of morphine failed to suppress self-administration behavior. Naloxone had no effects on cocaine reinforced responding. 20 references. (Author abstract modified)

001453 Sanger, D. J. Department of Psychology, University College, P.O. Box 78, Cardiff CF1 1XL, Wales **d-Amphetamine and adjunctive drinking in rats.** Psychopharmacology (Berlin). 54(3):273-276, 1977.

In the first of two experiments with d-amphetamine and adjunctive drinking, four food deprived rats developed high levels of adjunctive water drinking during daily sessions of intermittent food pellet delivery. When the water was removed and a solution of d-amphetamine sulfate put in its place, adjunctive drinking was disrupted towards the end of each session although the rats ingested doses of approximately 0.5mg/kg daily for over 40 sessions. Consumption of the d-amphetamine solution was increased by injections of several doses of alpha-methyl-para-tyrosine (AMPT). In a second experiment injections of d-amphetamine were found to reduce adjunctive water consumption in six rats. It was also found that the actions of the two highest doses of d-amphetamine were reduced by pretreatment with a dose of AMPT, which itself slightly reduced levels of drinking. These results suggest that, although adjunctive drinking may be a useful technique for inducing rats to self-administer d-amphetamine, the amount of drug consumed is limited by a direct action of the drug on drinking. 15 references. (Author abstract modified)

001454 Scheel-Kruger, Jorgen; Cools, Alexander R.; van Wel, Paul M. Psychopharmacological Research Laboratory, Sct. Hans Mental Hospital, Dept. E, DK-4000 Roskilde, Denmark **Muscimol a GABA-agonist injected into the nucleus accumbens increases apomorphine stereotypy and decreases the motility.** Life Sciences (Oxford). 21(11):1697-1702, 1977.

The effects of muscimol, a highly potent GABA agonist, on stereotypic behavior in rats was investigated. Muscimol (10ng and 100ng) when injected into the nucleus accumbens, was found to facilitate the development of stereotyped licking and gnawing, but contrastingly to depress the locomotion induced by subcutaneously injected apomorphine (0.25mg/kg). The local injection of muscimol alone induced no stereotypy. These results indicate that GABA in the nucleus accumbens differentially influences behavior dependent on dopaminergic mechanisms. 21 references. (Author abstract modified)

001455 Schlemmer, R. Francis, Jr.; Narasimhachari, Nedathur; Thompson, Valerie D.; Davis, John M. Department of Pharmacology, College of Medicine, University of Illinois Medical Center, Chicago, IL 60612 **The effect of a hallucinogen, 5-methoxy N,N-dimethyltryptamine, on primate social behavior.** Communications in Psychopharmacology. 1(2):105-118, 1977.

The behavioral effects of a hallucinogen, 5-methoxy N,N-dimethyltryptamine (5-MeODMT), were studied following acute and chronic administration of the substance to two selected members of a Stumptail macaque social colony of four adult monkeys. Intramuscular injection of 5-MeODMT in doses varying from 5 to 250micrograms/kg demonstrated dose dependent induction of abnormal behavior and attenuation of normal affiliative behavior. Abnormal behavior induced by 5-MeODMT included doglike wet shakes, involuntary limb jerks, stereotyped behavior, and hypervigilance. 5-MeODMT induced dose dependent decreases in social groom and initiated social activity while self-grooming either increased or remained unchanged. Dose dependent increases in submissive gesture were also seen following administration of the hallucinogen. Chronic administration of 250micrograms/kg 5-MeODMT for 12 days induced similar abnormal behavior and alterations of normal behavior. No definite signs of tolerance to any of these behavioral changes could be detected throughout the 12 day treatment period. Similarities of 5-DeODMT-induced behavioral changes in monkeys to the effect of this and other hallucinogens in humans are discussed. It is suggested that primate social colonies may offer an excellent paradigm to study the behavioral effects of hallucinogens as well as other psychotomimetics. 16 references.

001456 Schultz, Rudiger; Herz, Albert. Abteilung fur Neuropharmakologie, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munchen 40, Germany **Naloxone-precipitated withdrawal reveals sensitization to neurotransmitters in morphine tolerant/dependent rats.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 299(1):95-99, 1977.

Morphine tolerant/dependent rats were tested for their sensitivity to intracerebroventricularly (icv) administered putative neurotransmitters or other receptor agonists during naloxone precipitated withdrawal. Dopamine (DA), apomorphine, clonidine, and serotonin (5-hydroxytryptamine) reinitiated withdrawal jumping behavior when injected 30 minutes after naloxone. DA and apomorphine also reinitiated jumping, but to a lesser extent, when injected 3 hr after naloxone. Neither acetylcholine nor prostaglandin E-1 reinitiated withdrawal jumping. None of these substances induced jumping behavior in naive rats or in morphine tolerant/dependent rats before naloxone precipitated withdrawal. It is suggested that morphine tolerance and dependence may be associated with changes in the sensitivity of the central nervous system to putative neurotransmitter substances and that these changes are best demonstrated during the sudden termination of opiate action produced by administration of naloxone. 27 references. (Author abstract)

001457 Seidel, E. R.; Beaton, J. M.; Teague, R. S. Department of Pharmacology, University of Alabama, Birmingham, AL 35294 **The effects of oxotremorine and physostigmine on morphine-induced circling in the mouse.** Pharmacologist. 19(2):141, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the involvement of cholinergic receptors in morphine induced circling behavior in mice was reported. Mice were pretreated with oxotremorine or physostigmine prior to morphine. Neither oxotremorine nor physostigmine alone caused circling behavior. Mice treated with oxotremorine plus morphine circled significantly less than those receiving morphine plus saline. Physostigmine did not af-

fect morphine induced circling. It is suggested that muscarinic stimulation affects morphine induced circling. 1 reference. (Author abstract modified)

001458 Seliger, Deborah Levy. Department of Psychology, Rutgers – The State University, Camden, NJ 08102 **Passive avoidance learning in the rat as functions of d-amphetamine dosage and shock intensity.** Psychopharmacology (Berlin). 54(3):241-242, 1977.

The effects of d-amphetamine dosage and shock intensity on the learning of a passive avoidance response were assessed in rats. A curvilinear dose/response relationship was found at all shock levels, showing slower learning under moderate doses of d-amphetamine. The lowest shock level produced slower learning, especially in conjunction with the lowest dose of d-amphetamine. Results are discussed in terms of freezing behavior. 6 references. (Author abstract)

001459 Sette, William Francis. University of Rochester **Progressive force schedules in the squirrel monkey: effects of increment size, amphetamine, and haloperidol. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-25484 HC$15.00 MF$8.50 95 p.

Control of voluntary movement in four squirrel monkeys was investigated through a progressive force schedule of reinforcement, and the rate and dynamics of behavior were analyzed as a function of schedule parameters, amphetamine, and haloperidol. Under a minimum force criterion schedule, Ss worked at a steady rate across a wide range of criteria, emitted responses greater than criterion, were reinforced for at least 33% of their responses, and satisfied criteria approaching their bodyweight. Addition of tone signaling responses exceeding a lower limit criterion increased the percentage of reinforced responses and improved the relation between response force and criterion. Schedules with lower and upper limits (response bands) and upper limits were also used. Amphetamine led to increases in response output, total entrances into the response band, and decrease in percent of reinforced responses. Less effective doses increased response rate, force, and duration; more effective doses reduced these parameters. Haloperidol led to dose related decreases in response rate and an increase in multiple band entrance responses. Repetition of some doses abolished performance and produced overt hypokinetic effects. Subacute daily doses of haloperidol led to increases 24 hr after dose in response rate and total band entrances and decreases in percent of reinforced responses by the end of 1 wk in two Ss and 3 wk in a third. Overt hyperkinetic effects were seen in 2 Ss 2 to 6 hr following some doses. It is concluded that the new schedule provides an excellent but complex way of evaluating drug induced movement disorders, that the use of primates is critical in this area of research, and that use of nonessential neuroleptics should be curtailed. (Journal abstract modified)

001460 Shah, Nandkumar S.; Patel, V. O. Ensor Foundation Research Laboratory, William S. Hall Psychiatric Institute, Columbia, SC 29202 **Effects of psychotropic agents on amphetamine-induced behavior in rats.** Pharmacologist. 19(2):227, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of clozapine, molindone, pimozide, and levo-methadone on the iprindole mediated prolongation of the behavioral effects of dextroamphetamine in rats was reported. A single dose of amphetamine induced motor hyperactivity and stereotyped behavior lasting while a second later dose promptly restored the declining effects of the first dose. Iprindole markedly prolonged amphetamine induced stereotyped behavior and hyperactivity after the first dose; the prolonging effects were even longer after the second dose. Injection of clozapine or molindone prior to or after amphetamine produced no effect on amphetamine plus iprindole induced hyperactivity and stereotyped behavior. Levomethadone in a low dose prior to amphetamine had no effect, while at higher doses prevented responses to the first injection of amphetamine only. Preinjection or postinjection treatment with pimozide completely prevented or blocked the amphetamine or amphetamine plus iprindole mediated locomotor hyperactivity and stereotyped behavior. (Author abstract modified)

001461 Sheard, Michael; Astrachan, David; Davis, Michael. Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06508 **Tricyclic antidepressant drugs: antagonism of effect of D-lysergic acid diethylamide (LSD) on shock elicited aggression.** Communications in Psychopharmacology. 1(2):167-173, 1977.

The effect of tricyclic antidepressant drugs on shock elicited aggression (SEA) of rats receiving D-lysergic acid diethylamide (LSD) was examined in a study in which the SEA of 60 male rats was observed before and after the administration of chlorimipramine (CIMI) and desipramine (DMI). Pretreatment of rats with single doses of the tricyclic antidepressant drugs CIMI and DMI was found to markedly antagonize the excitatory effect of LSD on shock elicited aggression. CIMI and DMI by themselves in single doses do not significantly affect SEA. The results are discussed in terms of the serotonin hypothesis of the action of hallucinogenic drugs on single neurons and behavior. 15 references. (Author abstract modified)

001462 Shearman, Gary; Hynes, Martin; Fielding, Stuart; Lal, Harbans. Department of Pharmacology and Toxicology, University of Rhode Island College of Pharmacy, Kingston, RI 02881 **Clonidine self-administration in the rat: a comparison with fentanyl self-administration.** Pharmacologist. 19(2):171, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study comparing clonidine self-administration and fentanyl self-administration in the rat was reported. Rats were implanted with chronic indwelling jugular catheters and trained to lever press in order to obtain the drug. Fentanyl and clonidine were readily self-administered. Stable rates of lever pressing were obtained in about 5 da. Self-administration was not acquired when the doses were one tenth of the maximum. Lever pressing increased when 3 presses or 10 presses were required for each injection. Twenty percent of the clonidine self-administering rats died. Clonidine in high doses but not low doses, could maintain self-administration behavior in the fentanyl self-administering animals when clonidine was substituted for fentanyl. (Author abstract modified)

001463 Sietnieks, A.; Meyerson, B. J. Department of Medical Pharmacology, University of Uppsala, Uppsala, Sweden **The influence of progesterone on the inhibitory effect of lysergic acid diethylamide on copulatory behaviour in the female rat.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):75, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the influence of progesterone (PRO) on the inhibitory effect of lysergic acid

diethylamide (LSD) on copulatory behavior in the ovariectomized rat (lordosis response on mounting by a male) was studied. Different doses of PRO were given after estradiol benzoate and before LSD treatment. The LSD action was not influenced by different doses of estradiol, but was enhanced with increasing doses of PRO. The results suggest an interaction of PRO on the lordosis inhibitory actions of LSD.

001464 Smee, M. L.; Overstreet, D. H. Flinders University of South Australia, School of Biological Sciences, Bedford Park, South Australia 5042, Australia **Biphasic effects of apomorphine on locomotor activity in rats.** Communication in Psychopharmacology. 1(2):99-104, 1977.

The effects of apomorphine (0.75, 1.5, and 3.0mg/kg) on locomotor activity in rats was observed over a 2 min period at 30 and 150 min following injection. All doses of the drug produced predominantly stereotyped behavior (licking and sniffing) at 30 min after injection. Depressed activity was observed at 150 min, the degree of depression being greater for 3.0mg/kg than for 0.75mg/kg. These biphasic effects of apomorphine are opposite in nature to those produced by high doses of morphine and may be dependent upon similar but converse changes in the dopaminergic system. 17 references. (Author abstract)

001465 Stanton, D.; Paule, M.; Weinberger, S. B. Department of Pharmacology, University of California at Davis School of Medicine, Davis, CA 95616 **Disruption of learning performance by chronic chlorpromazine administration in the baboon.** Pharmacologist. 19(2):228, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of chronic chlorpromazine administration on the acquisition of learning new sequences of lever pressing in the epileptic baboon, Papio papio, was reported. Chlorpromazine produced dose related decrease in learning ability which did not appear to result from motor difficulties. The decrease in performance was manifested by slower performance and, at the highest dose, failure to attempt the task. Decreased efficiency was particularly marked. Both short-term and long term tolerance to chlorpromazine occurred. Chlorpromazine administration also induced dose related increases in seizure susceptibility to flashing light over the course of the experiment, with rapid recovery to normal responsiveness following the last dose. (Author abstract modified)

001466 Stephens, D. N.; Herberg, L. J. Institute of Neurology, National Hospital, Queen Square, London WC1N 3BG, England **Effects on hypothalamic self-stimulation of drugs influencing dopaminergic neurotransmission injected into nucleus accumbens and corpus striatum of rats.** Psychopharmacology (Berlin). 54(1):81-85, 1977.

The roles of the nucleus accumbens septi (ACB) and corpus striatum (CPU) in rat self-stimulation were investigated by injecting directly or indirectly acting stimulant drugs or a dopamine (DA) receptor blocking agent into each site bilaterally. d-Amphetamine facilitated hypothalamic self-stimulation when injected into either site. Apomorphine depressed or facilitated responding, the direction and magnitude of this effect being contingent on the effect of systemic injection, and correlated with the difference between the effects of d-amphetamine and l-amphetamine but not with injection site. Haloperidol in either site depressed self-stimulation. Tyramine, an agent believed to cause noncontingent displacement of transmitter from catecholamine terminals, depressed self-stimulation when injected into the CPU, but facilitated it when injected into the ACB. The site specific effects found with tyramine but not with apomorphine may have been due to release by tyramine of transmitters other than DA. 21 references. (Author abstract modified)

001467 Steranka, L. R.; Barrett, R. J.; Sanders-Bush, Elaine. Tennessee Neuropsychiatric Institute, Nashville, TN **Facilitation of Sidman avoidance performance by para-chloroamphetamine: role of biogenic amines.** Neuropharmacology (Oxford). 16(11):751-759, 1977.

A series of experiments was designed to test the extent to which the catecholamines and serotonin (5-HT) mediate the facilitatory effects of para-chloroamphetamine (PCA) on non-discriminated barpress (Sidman) avoidance performance in rats. The administration of 5mg/kg of PCA to trained rats produced a dramatic increase in avoidance responding which gradually dissipated over 8 hr. No additional effect was observed during 10 daily 4 hr test sessions, although brain levels of 5-HT were still reduced 48 hr after the last test session. The optical isomers of PCA are equipotent with regard to their initial effects on brain 5-HT mechanisms; however, (S)-(+)-PCA was more potent than (R)-(-)-PCA in the behavioral task as well as in the ability to increase in vivo tyrosine hydroxylase activity and increase the rate of conversion of 3H-tyrosine to 3H-catecholamines. Moreover, the facilitatory effect of PCA on Sidman avoidance performance, in contrast to the stimulatory effect of the drug on motor activity, did not diminish significantly after three daily administrations of 5mg/kg. These results indicate that PCA produces an amphetamine like facilitatory effect on behavior which is independent of its effects on 5-HT mechanisms and is related to drug induced changes in the metabolism of catecholamines in brain. 34 references. (Author abstract modified)

001468 Stowe, Judith Ellen. North Texas State University **The effects of stimulation and depression of the reticuloendothelial system on Sidman avoidance behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-19685 HC$15.00 MF$8.50 87 p.

The role of the reticuloendothelial system (RES), which functions in immunological reactions and other homeostatic protective functions, was investigated in ongoing Sidman avoidance behavior of male rats. Experimental Ss were injected with either a RES depressant or stimulant, and interval measurements were taken to ensure that predicted RES changes were occurring and maintained. Results indicated that RES stimulated Ss showed significant deterioration in avoidance performance as compared to other experimental and control groups. Stimulated Ss were also poorer in Sessions 2 and 3, but these results were not significant. A rank order correlation revealed that a significant negative correlation existed between RES stimulation and avoidance performance, based on changes in RES levels from baseline to the end of the shock program. Findings suggested that increased stress resistance due to RES stimulation may reduce the aversive properties of the shock program, thus decreasing motivation for responding. It was concluded that artificial methods of inducing stress resistance by RES stimulation may be a useful therapeutic technique for patients experiencing psychological stress. (Journal abstract modified)

001469 Stretch, Roger. Behavioral Pharmacology Research Unit, University of Ottawa, 1245 Kilborn Ave., Ottawa, Ontario K1N 6N5, Canada **Discrete-trial control of cocaine self-injection behaviour in squirrel monkeys: effects of morphine,**

nalaxone, and chlorpromazine. Canadian Journal of Physiology and Pharmacology (Ottawa). 55(4):778-790, 1977.

Intravenous cocaine self-injection behavior was studied using a new discrete trials procedure in monkeys. Daily sessions consisted of two sets of 40 discrete trials, separated by a 5 min time out period; the intertrial interval during each segment of the session was equal to 50 s. When cocaine self-injection responding was suppressed by morphine pretreatment, the morphine antagonist, naloxone, reinstated drug taking behavior. When monkeys were pretreated with chlorpromazine before a cocaine self-injection session, small doses marginally increased responding and larger doses exerted a suppressive effect. When the dose of cocaine was increased, small doses of chlorpromazine (0.03 to 1mg/kg) exerted no clearly detectable effects, though responding for drug injections was profoundly suppressed when sessions were preceded by chlorpromazine pretreatment at doses of 3 and 5.6mg/kg. When considered in relation to the results of other experiments, it is evident that control of cocaine self-injection responding by a discrete trials procedure results in schedule dependent behaviors that differ in relative sensitivity to drug pretreatments from cocaine reinforced responding controlled by fixed ratio schedules of drug reinforcement. 43 references. (Author abstract modified)

001470 Stretch, Roger. Faculty of Psychology, University of Ottawa, Ottawa, Ont. K1N 6N5, Canada **Discrete-trial control of morphine self-injection behaviour in squirrel monkeys: effects of naloxone, morphine, and chlorpromazine.** Canadian Journal of Physiology and Pharmacology (Ottawa). 55(3):615-627, 1977.

Intravenous morphine self-injection behavior was studied using a new discrete trials procedure in monkeys. When daily sessions consisted of 40 trials at an intertrial interval of 50 seconds, morphine self-injection behavior was neither increased nor consistently decreased by naloxone pretreatment. When monkeys were pretreated with morphine before a given session, responding for drug injections was suppressed. The effect was reversed by naloxone which, if injected at time out period, reinstated morphine self-administration behavior. When an injection of chlorpromazine preceded a given session, responding for morphine injections was also suppressed. Naloxone failed to reinstate chlorpromazine suppressed responding, indicating that naloxone acted as an acute morphine antagonist under some circumstances, but did not otherwise influence behavior. Though small increases in morphine intake were observed after naloxone pretreatment, substantial increases in response output during the intertrial interval, with a consequent loss of stimulus control normally exerted by the trial signal, were observed. These results were interpreted in terms of acute, antagonist precipitated withdrawal signs, not evident in response to naloxone pretreatment when drug self-injection responding was maintained on a daily basis by a limited number of smaller unit injection doses of morphine. 23 references. (Author abstract modified)

001471 Tache, Y.; Lis, M.; Collu, R. Universite de Montreal, Montreal, Quebec, Canada **Effects of thyrotropin-releasing hormone on behavioral and hormonal changes induced by beta-endorphin.** Life Sciences (Oxford). 21(6):841-846, 1977.

The possibility of an antagonizing effect of thyrotropin releasing hormone (TRH) on beta-endorphin induced behavioral and hormonal changes in rats, as well as in vitro TRH effect on stereospecific opiate binding was investigated. Adult male rats were injected intraventricularly either with saline or TRH (10 micrograms) 5 min prior to a second injection of either saline or beta-endorphin (50 micrograms). The tripeptide produced a 100% increase of motility counts recorded over a 15 min period following the last injection, whereas beta-endorphin decreased general motor activity. TRH pretreatment completely abolished the depressant effect of beta-endorphin. These results do not seem to be related to an interaction of TRH with opiate receptors since the tripeptide added in vitro to rat brain homogenates did not alter the specific binding of 3H-naloxone nor affect the displacement by beta-endorphin of such binding. 29 references. (Journal abstract modified)

001472 Thiebot, M. H.; Soubrie, P.; Chermat, R.; Simon, P.; Boissier, J. R. Unite de Recherches de Neuropsychopharmacologie de L'INSERM, 2 rue d'Alesia, F-75014 Paris, France **/Behavioral and psychopharmacological characteristics of rats raised in high population density./ Caracteristiques comportementales et psychopharmacologiques de rats eleves en haute densite de population.** Psychopharmacology (Berlin). 54(3):283-288, 1977.

In a study of the effects on rats of rearing under conditions of high population density, behavioral and pharmacological tests were performed on rats maintained either during 6 weeks at 20 or five in a cage (40x40x17 cm) or during 6 weeks at 20 and during 8 days at five in a cage. When compared to five/cage reared rats, overcrowded rats (20/cage) exhibit a lessened locomotor activity in the open field, staircase test, and Y-maze; rearings, intrasession habituation, and spontaneous alternation were not altered. It seems difficult to relate this lessened locomotor activity to an enhanced emotionality level. Although overcrowded rats showed heavier adrenals, their susceptibility to restraint induced gastric ulcers, their "neophobic" responses to new food, and their sensitivity to the stimulating effect of oxazepam in the Y-maze were not modified. Sensitivity to amphetamine induced stereotyped behavior and to pentobarbital induced hypnosis was found to be increased in overcrowded rats. Apomorphine induced stereotypy and barbital sleeping time were not modified. All these data (except the fact that barbital onset of hypnosis was delayed in overcrowded rats) may suggest an altered hepatic metabolism in rats reared at 20 in a cage. In overcrowded rats an enhanced amphetamine induced stereotyped behavior was associated with a lessened locomotor activity. Moreover, after 8 days at five in a cage, this increased sensitivity to amphetamine (and to pentobarbital) completely disappeared, whereas locomotor activity was not fully restored. This suggests that amphetamine sensitivity is not related to the predrug activity level of the animals. 16 references. (Author abstract modified)

001473 Thompson, Donald M. Dept. of Pharmacology, Georgetown University School of Medicine, Washington, DC 20007 **Effects of cocaine and fenfluramine on progressive-ratio performance.** Pharmacology Biochemistry & Behavior. 7(6):555-558, 1977.

The effects of cocaine and fenfluramine on pigeons' performance on a progressive ratio schedule that required eight additional responses for each successive reinforcement were examined. The number of responses in the final ratio of the session was defined as the breaking point. When cocaine was administered, the breaking point increased and then decreased as a function of increasing doses (0.3to 10mg/kg). In contrast, across the same range of doses of fenfluramine, the breaking point only decreased. At doses of each drug that decreased the breaking point, the high running rate of responding was interrupted by pauses. At doses of cocaine that increased the breaking point, the running rate was also disrupted, but the

disruption was characterized by lower, irregular rates rather than pausing. The increases in breaking point observed at 3mg/kg of cocaine were no longer seen when fenfluramine was administered at the same time. The possibility is raised that fenfluramine might be a useful blocking agent in the treatment of cocaine abuse. 25 references.

001474 Thompson, Donald M. Georgetown University School of Medicine and Dentistry, Washington, DC 20007 **Development of behavioral tolerance to cocaine.** Pharmacologist. 19(2):231, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the development of behavioral tolerance to cocaine, as measured by determining the effects of the drug on operant responding in pigeons, was reported. The pigeons obtained food by making four responses on three keys in a specific sequence. Errors produced brief timeout periods, during which the keylights were off and responses had no effect. Cocaine administration increased total errors, increased the relative frequency of nonswitching errors (perseveration), decreased the rate of within session error reduction (learning), and increased the total trial time (pausing). Over 30 to 50 sessions during which cocaine was administered repeatedly, these effects disappeared. Tolerance did not develop, however, to cocaine induced increases or decreases in timeout responding. Such effects were nondisruptive in that they did not reduce the rate of food reinforcement. Cocaine was also studied in a performance condition, in which the sequence of correct responses was the same in each session. Cocaine increased performance errors and produced pausing, but tolerance to this effect developed more quickly than in the learning condition. (Author abstract modified)

001475 Tikal, K. Pharmacological Dept., Charles University, Srobarova 50, 100 42 Praha 10, Czechoslovakia **The effect of noradrenaline on the ECoG of the preparation encephale isole of rats.** Activitas Nervosa Superior (Praha). 19(2):102-103, 1977.

The effect of noradrenaline (NA) on the electrocorticogram (ECoG) of the preparation encephale isole of rats was determined by administering NA intravenously to elicit a two phase ECoG response in freely moving rats, and studying resulting ECoG amplitudes. NA elicited in the preparation encephale isole of rats a short, rapidly disappearing arousal reaction, which was mostly detectable only after the first administration. Further NA injections in regular 15 min intervals did not elicit activation, but merely a decrease in the mean amplitude of ECoG. These findings indicate that a direct central as well as an indirect reflexly mediated peripheral effect presents in the mechanism of the activating ECoG phase of noradrenaline action. 8 references.

001476 Tortella, F. C.; Moreton, J. E.; Khazan, Naim. Department of Pharmacology and Toxicology, University of Maryland School of Pharmacy, Baltimore, MD 21201 **EEG and behavioral effects of D-ala2-meth-enkephalinamide in the rat.** Pharmacologist. 19(2):189, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study comparing the electroencephalographic (EEG) and behavioral effects in rats of intraventricularly administered D-enkephalin, morphine, and/or naloxone was reported. Naloxone alone had no effects on EEG. Both D-enkephalin and morphine produced a biphasic response of EEG slow bursts and behavioral stupor followed by EEG and behavioral arousal. The EEG slow bursts and behavioral stupor occurred 5 min to 20 min after administration and persisted to 60 min to 90 min following administration of either drug. The mean integrated EEG voltage output associated with EEG synchrony during behavioral stupor was increased to about 250% of control after D-enkephalin and to about 200% of control after morphine. The peak increase in EEG voltage output occurred earlier with D-enkephalin. Naloxone antagonized both morphine and D-enkephalin effects. (Author abstract modified)

001477 Trulson, Michael E.; Stark, Arlene D.; Jacobs, Barry L. Department of Psychology, Princeton University, Princeton, NJ 08540 **Comparative effects of hallucinogenic drugs on rotational behavior in rats with unilateral 6-hydroxydopamine lesions.** European Journal of Pharmacology (Amsterdam). 44(2):113-119, 1977.

Dopaminergic actions of various hallucinogenic drugs were compared by examining their effects on rotational behavior in rats with unilateral 6-hydroxydopamine lesions of the nigrostriatal pathway. LSD produced strong contralateral turning, indicating that it is a potent dopamine receptor agonist, while 2-bromo-d-lysergic acid diethylamide bitartrate was found to be weak dopamine receptor agonist. 2,5-Dimethoxy-4-methylamphetamine HCl (STP) and mescaline produced significant ipsilateral turning, indicating that these compounds have moderate dopamine releasing action. All the following drugs produced a small amount of ipsilateral turning. N,N-dimethyltryptamine-HCl (DMT), 5-M-DMT, tryptamine, scopolamine, and psilocin. Results suggest that although a dopaminergic effect is not a necessary property of hallucinogenic drugs, the ability to activate dopamine receptors may be an important factor in determining the potency of hallucinogenic drugs. 26 references. (Journal abstract modified)

001478 Tye, Nicholas C.; Horsman, Linda; Wright, Francesca C.; Large, Bruce T.; Pullar, Ian A. Lilly Research Centre Limited, Erl Wood Manor, Windlesham, Surrey, England **Two dopamine receptors: supportive evidence with the rat rotational model.** European Journal of Pharmacology (Amsterdam). 45(1):87-90, 1977

To investigate the ability of haloperidol and clozapine to block the turning behavior induced by the dopamine agonists, diisobutyryl apomorphine and lergotrile, 6-hydroxydopamine lesioned (at the level of the substantia nigra) rats treated with apomorphine ester or lergotrile followed by haloperidol or clozapine were assessed for turning behavior at 15 min intervals. Haloperidol (1.5and 3.0mg/kg p.o.)blocks the rotational behavior due to the apomorphine ester but has no effect on lergotrile turning. Clozapine blocks the lergotrile turning but stimulates the rotational behavior produced by the apomorphine ester. The results support the concept of two anatomically separate dopamine receptors and their relevance to the study of antipsychotic activity is discussed. 10 references. (Author abstract modified)

001479 Urba-Holmgren, Ruth; Holmgren, Bjorn; Aguiar, Margarita. Centro Nacional de Investigaciones Cientificas, Apartado 6990, La Habana, Cuba **Circadian variation in am amphetamine induced motor response.** Pharmacology Biochemistry & Behavior. 7(6):571-572, 1977.

Significant diurnal variation in occurrence and duration of d-amphetamine induced head shaking were observed in 9 day old rats. The lowest values were obtained near noon, and the highest around midnight. These variations should be considered if head shaking is to be used as a quantitative neuropharmacological test. 9 references. (Author abstract)

001480 Valdman, A. V.; Kozlovskaya, Marina M. Dept. of Pharmacology, Pavlov Medical Institute, Leningrad, USSR **Psychotropic drug effects on the emotional state of cats in a social situation.** Activitas Nervosa Superior (Praha). 19(3):222-224, 1977.

In a paper presented at the second international CIANS congress, the use of psychotropic drugs for analysis of spontaneous and experimentally changed emotional states of free moving cats in a social situation is reported. Zoosocial contacts and responses to food, pain, and various test stimuli were registered, and blood pressure, heartrate, muscle tone, and electrical skin resistence were recorded. Psychotropic drugs affected the emotional behavior when administered in doses lower than those affecting expression movements and autonomic changes. Pharmacological dissociation between the emotional expression and emotional state is suggested.

001481 Vasko, Michael; Carney, John. Veterans Administration Hospital, Dallas, TX 75216 **Barbital induced tolerance and cross tolerance to various CNS depressants on rat operant behavior.** Pharmacologist. 19(2):175, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of various CNS depressants on rat operant behavior and of the induction by barbital of tolerance and cross-tolerance to these effects was reported. In rats trained to respond under a variable interval (VI) schedule of water reinforcement, intraperitoneal (ip) injections of barbital, diphenylhydantoin, pentobarbital, and ethanol produced increases in VI responding. Higher doses of each drug caused a decrease in responding. Tolerance to barbital was induced by injections of barbital daily for three weeks. This dose of barbital initially decreased VI responding to 25% of control. Tolerance to both the stimulant and the depressant effects of barbital on response rate developed. Cross-tolerance for both rate increasing and rate decreasing effects of diphenylhydantoin, pentobarbital, ethanol, and methadone was observed in barbital tolerant rats; doses of these drugs that decreased responding in nontolerant rats increased responding in tolerant animals. (Author abstract modified)

001482 Velkov, V. no address **On the effect of Nootropil an ATP and ATPase in brain of rats.** Studia Psychologica (Bratislava). 19(3):264, 1977.

Increased ATP content and the ATPase activity in the brain of aged rats to about the level in young rats by chronic doses of 100mg/kg Nootropil (piracetam) for 15 days is reported. A utilization of the energy supplied by the ATP is seen to result in increased memory with an increased macromolecular biosynthesis of nucleotid acids, proteins, and lipids. It is suggested that the increased ATP content and ATPase activity caused in the animal's brain by Nootropil has significance for the electric neuroconductivity and memory formation. (Author abstract modified)

001483 Vogt, Marthe. Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **Histamine H2-receptors in the brain and sleep produced by clonidine.** British Journal of Pharmacology (London). 61(3):441-443, 1977.

To determine if sleep produced by clonidine results from stimulation of histamine H2 receptors in the brain, sleep was induced in chicks aged 4 to 7 days by intravenous injection of clonidine hydrochloride 0.04 micromole/kg. Sleep was not prevented or altered by a preceding intramuscular injection of blockers of histamine H2 receptors which were used in doses (as micromole/kg) of up to 800 (metiamide) and 2400 (cimetidine). Clonidine, therefore, does not cause sleep by stimulating H2 receptors in the brain. The highest dose of cimetidine used had a hypnotic action of its own. 8 references. (Author abstract modified)

001484 Voith, Katherine. Dept. of Pharmacology, Ayerst Research Labs., Montreal H3C 3J1, Canada **Comparison of behavioral supersensitivity to apomorphine after fluphenazine dihydrochloride and fluphenazine decanoate treatment in rats.** Progress in Neuro-Psychopharmacology. 1(3/4):289-295, 1977.

Experiments were undertaken to compare the duration of supersensitivity to dopaminergic stimulation after chronic oral treatment with fluphenazine dihydrochloride and after a single injection of fluphenazine decanoate. After cessation of fluphenazine dihydrochloride treatment both the intensity and the duration of stereotypy, in response to apomorphine, were significantly enhanced. The supersensitivity lasted for about 4 weeks. After fluphenazine decanoate, apomorphine induced stereotypy and open-field behavior were either absent or significantly depressed for 4 to 5 weeks. At 6 weeks, the intensity of stereotypy was enhanced and ambulation significantly elevated. The supersensitivity lasted for less than 2 weeks. The finding that increased receptor sensitivity was of shorter duration after depot neuroleptic treatment suggests that tardive dyskinesia is less likely to develop in response to long-acting antipsychotic drugs. 24 references. (Author abstract)

001485 Weiner, William J.; Goetz, Christopher; Nausieda, Paul A.; Klawans, Harold L. Dept. of Neurological Sciences, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612 **Clonazepam and dopamine-related stereotyped behavior.** Life Sciences (Oxford). 21(7):901-905, 1977.

The effect of clonazepam on behavioral stereotypy induced by a number of dopaminergic agonists was investigated in guinea-pigs. Clonazepam inhibited levodopa and amphetamine induced behavior in guinea-pigs but did not alter lergotrile or apomorphine induced stereotypy. The results suggest that clonazepam influences the central dopaminergic system through a direct effect of dopaminergic presynaptic mechanisms. 18 references. (Journal abstract)

001486 Weinstock, Marta; Zavadil, A. P.; Rosin, A. J.; Chiueh, C. C.; Kopin, I. J. Laboratory of Clinical Science, NIMH, 9000 Rockville Pike, Bldg. 10, Room 2D-46, Bethesda, MD 20014 **Peripheral catecholamines released by oxotremorine modulate tremor in the rat. (Unpublished paper).** Bethesda, MD, NIMH, 1977. 1 p.

The effect of peripheral catecholamines released by oxotremorine on tremor in the rat was investigated. Oxotremorine produced a whole body tremor in rats which was abolished by scopolamine and was reduced in intensity by l-propranolol. D-propranolol and sotalol were less active in reducing intensity of the tremor. Adrenalmedullectomy or depletion of peripheral norepinephrine by intravenous 6-hydroxydopamine reduced tremor intensity by half. Plasma levels of epinephrine and norepinephrine were increased four fold following oxotremorine injection, but propranolol did not prevent this rise in plasma catecholamines. It is suggested that stimulation of central muscarinic receptors results in at least two effects which influence tremor: 1) an increase in cholinergic drive to motor efferents and 2) activation of the sympathoadrenalmedullary system with release of catecholamines that augment tremor by an action mediated by beta-adrenoceptors. (Author abstract modified)

001487 Wetzel, W.; Ott, T. Institute of Pharmacology, Medical Academy, Magdeburg, Germany **Effect of scopolamine on retention of a shock-motivated brightness discrimination in rats.** Activitas Nervosa Superior (Praha). 19(2):121-122, 1977.

In a paper delivered at the Second International CIANS Congress (Prague), an investigation of the effect of scopolamine on retention of learned information is presented. Adult male Wistar rats were trained to perform a shock motivated brightness discrimination in a semiautomatic Y-chamber in 40 consecutive trials, with retention tested at different times after the training in a relearning experiment. Scopolamine (0.5mg/kg) significantly improved retention after 24 h. The effect of scopolamine was dependent not only on dosage but also on training performance. It is suggested that hippocampal cholinergic synapses are responsible for the cholinolytic effects on the retention of brightness discrimination. 2 references.

001488 Wharton, Walker; McMillan, D. E. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Effects of d-amphetamine on different rates of avoidance behavior in rats.** Pharmacologist. 19(2):227, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of dextroamphetamine on the rates of avoidance responding in rats at different response/shock intervals (RSI) was reported. During the first exposure to an RSI of 10 sec, dextroamphetamine increased response rates in a dose dependent manner. In the same animals, when the RSI was decreased to 1 sec, the response rate increased while dextroamphetamine decreased rates of responding at doses greater than 0.3mg/kg. When the RSI was returned to 10 sec, the response rate in the same animals was much higher than that previously observed under this schedule. Dextroamphetamine produced only small rate decreases at low doses and decreased rates at higher doses. It is suggested that drug effects of avoidance responding at a particular RSI can be influenced by the behavioral history of the animal through rate dependent mechanisms. (Author abstract modified)

001489 White, F. J.; Kuhn, D. M.; Appel, J. B. Behavioral Pharmacology Laboratory, Department of Psychology, University of South Carolina, Columbia, SC 29208 **Discriminative stimulus properties of quipazine.** Neuropharmacology (Oxford). 16(12):827-832, 1877.

To investigatate the stimulus properties of 2-piperazinyl quinoline (quipazine) and its mechanism of action, rats were trained to discriminate quipazine (2.5mg/kg) from saline in a two lever, drug discrimination task. After high levels of accuracy (i.e. 90% correct choice responding) were attained, dose and time parameters of the quipazine cue were studied during extinction test sessions. Quipazine was highly discriminable at doses of 1.25 and 0.94mg/kg. With decreasing doses, the percentage of responding on the quipazine lever declined in a dose related fashion. By varying the normal 30min time interval between injection and testing, the onset and duration of action of quipazine were determined to be about 5 to 15 min and 60 to 90 min respectively. After injections with novel drugs, animals were tested during extinction sessions. Lysergic acid diethylamide, (LSD), at doses of 0.08mg/kg and 0.10mg/kg, transferred completely to the quipazine cue (i.e. above 95% quipazine responding); neither D-amphetamine nor apomorphine (0.5and 1.0mg/kg showed any transfer to the quipazine cue. It was found that the putative central serotinin (5-HT) antagonists cyproheptadine, methysergide, and methiothepin produced significant decreases in the descriminability of quipazine. The dopamine (DA) is antagonists haloperidol and fluphenazine were without effect. It concluded that LSD and quipazine have a common mechanism of action which may (or may not) involve 5-HT; a role for DA was not indicated. 21 references. (Author abstract modified)

001490 Wiegant, Victor M.; Cools, Alexander R.; Gispen, Willem Hendrik. Division of Molecular Neurobiology, Rudolf Magnus Institute for Pharmacology, Padualaan 8, Utrecht, The Netherlands **ACTH-induced excessive grooming involves brain dopamine.** European Journal of Pharmacology (Amsterdam). 41(3):343-345, 1977.

The possible involvement of brain dopamine in ACTH induced excessive grooming was studied in male Wistar rats. Ten days prior to the experiments, cannulae were implanted in the intraventricular foramen and the neostriatum or the substantia nigra. Intraventricular injection of ACTH(1-24) 15 min before observation induced excessive grooming, which was suppressed by haloperidol i.p. 60 min prior to observation or by fluphenazine s.c. 60 hr prior to observation. Ongoing behavior of control rats was not affected by haloperidol alone or fluphenazine alone. Bilateral neostriatal injection of haloperidol 15 min before observation also suppressed grooming behavior induced by ACTH(1-24) injected intraventricularly, but bilateral neostriatal injection of haloperidol alone did not affect grooming activity. Bilateral injection of ACTH(1-24) into the substantia nigra 15 min before observation elicited grooming, but bilateral injection of haloperidol into the substantia nigra did not suppress grooming induced by intraventricular ACTH(1-24). Since ACTH(1-24) injection was ineffective in the neostriatum but effective in the substantia nigra, a nigrostriatal dopamine pathway may be involved. A common dopaminergic component may be involved in ACTH induced and morphine induced behavior. 5 references.

001491 Willner, P. J.; Crowe, R. Psychology Department, City of London Polytechnic, Old Castle Street, London E1 7NT, England **Effect of chlordiazepoxide on the partial reinforcement extinction effect.** Pharmacology Biochemistry and Behavior. 7(5):479-482, 1977.

To examine the effect of chlordiazepoxide on the partial reinforcement acquisition/extinction effects, rats were trained to run in a straight alley under conditions of partial or continuous reinforcement. Extinction was slower after partial reinforcement. Chlordiazepoxide, administered during acquisition only, had no effect on acquisition but abolished the partial reinforcement extinction effect. The results support the hypothesis that chlordiazepoxide acts by attenuating the effects of aversive stimuli. 36 references. (Author abstract modified)

001492 Wilson, M. C. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **The effect of cocaine and d-amphetamine on punished responding.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 227(1):98-105, 1977.

Effect of cocaine and d-amphetamine on punished responding was investigated in the rat. Various doses of d-amphetamine (0.1, 0.5, and 2.5mg/kg) and cocaine (5, 20, and 40mg/kg) were administered i.p. to 7 rats trained in an experimentally induced conflict procedure. Cocaine (5mg/kg and 20mg/kg) and d-amphetamine (0.5and 2.5mg/kg) significantly decreased responding in both punished and unpunished periods. Following these treatments the rate of responding in

punished and unpunished components was not significantly different. Findings suggest that psychomotor stimulants may not selectively increase anxiety, at least at doses which are not at the same time anorexic. 9 references. (Journal abstract modified)

001493 Wilson, M. C.; Bellarosa, A.; Bedford, J. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Sociopharmacology of d-amphetamine in Macaque arctoides II.** Pharmacologist. 19(2):227, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects on group behavior of administration of dextroamphetamine of saline in a randomized sequence to each member of a heterosexual group of Macaque arctoides monkeys was reported. Prior to the observation period a competitive food test was conducted in order to ascertain social dominance/drug interactions. The results were similar to those previously reported following acute administration of dextroamphetamine to induvidual members of a group of monkeys. Social grooming and playing were decreased at the higher dosages; however, heterosexual presenting and vocalization increased. Males exhibited signs of sexual arousal but mounting did not increase. An interaction between dominance and drug effect was noted in the feeding test. Since only low ranking animals would successfully compete for food following treatment with anorexic dosages of dextroamphetamine. 1 reference. (Author abstract modified)

001494 Wilson, Marvin C. Dept. of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Pharmacological modification of shock potentiated amphetamine lethality.** European Journal of Pharmacology (Amsterdam). 44(4):365-374, 1977.

The ability of the acute application of inescapable footshock to potentiate d- and d,l-amphetamine in rodents is confirmed and a similar interaction with l-amphetamine is examined. Aggregation further enhanced this potentiation. Prior subacute exposure to shock did not prevent the potentiated lethality. Shock potentiated amphetamine lethality was antagonized by pretreatment with agents which indirectly reduce catecholamine release (6-hydroxydopamine, alpha-methyl-p-tyrosine) and by bilateral adrenalectomy. Antagonism did not result from pretreatment with the adrenergic blocking agents propranolol and phenoxybenzamine nor with methoxamine and hydrocortisone. Pretreatment with haloperidol and pentobarbital completely antagonized the potentiated lethality whereas morphine and fenfluramine pretreatment did not. Shock potentiated amphetamine lethality was enhanced by pretreatment with physostigmine and neostigmine but was antagonized by methylatropine. However atropine pretreatment enhanced lethality. It would appear that the release of norepinephrine from the brain and/or the adrenal medulla either is directly involved in mediating amphetamine lethality or in mediating the effects of acute physical stress on amphetamine's lethal actions. 15 references. (Author abstract modified)

001495 Wise, Roy A.; Yokel, Robert A.; Hansson, Peter A.; Gerber, Gary J. Department of Psychology, Room H1060, Concordia University, 1455 de Maisonneuve Boulevard, West, Montreal H3G 1M8, Canada **Concurrent intracranial self-stimulation and amphetamine self-administration in rats.** Pharmacology Biochemistry and Behavior. 7(5):459-461, 1977.

To examine the effect of concurrent intracranial stimulation and amphetamine self-administration on rate of responding, and to determine whether amphetamine stereotypy interferes with lever pressing for stimulation, rats were given concurrent access to intravenous amphetamine and brain stimulation reinforcers in a two lever test chamber. Responding for each reinforcer was generally increased above baseline rates taken when only one reinforcer was available. Amphetamine stereotypy was observed, but did not interfere with rapid lever pressing for brain stimulation. 12 references. (Author abstract modified)

001496 Wojcik, M.; Mitros, K.; Jastreboff, P. J.; Zielinski, K. Nencki Institute of Experimental Biology, Warsaw, Poland **The lack of effect of synthetic scotophobin on darkness avoidance in mice.** Activitas Nervosa Superior (Praha). 19(2):163-165, 1977.

A paper delivered at the Second International CIANS Congress (Prague), concerned with the controversy around the experiments of Ungar which apparently show that scotophobin can induce dark avoidance in mice, is presented. On the basis of a series of experiments exactly reproducing Ungar's it was concluded that the behavior of noninjected mice was highly variable from trial to trial and that dark box time (DBT) is not a reliable measure of the behavior of individual subjects. A further finding showed that activity and DBT were negatively correlated and this suggests that Ungar's findings may result from increases in activity following scotophobin treatment. 4 references.

001497 Worms, Paul; Scatton, Bernard. Synthelabo-LERS, Department of Biology, Neuropharmacology Unit, 31, avenue Paul Vaillant Couturier, F-92220 Bagneux, France **Tolerance to stereotyped behaviour and to decrease in striatal homovanillic acid levels after repeated treatment with apomorphine dipivaloyl ester.** European Journal of Pharmacology (Amsterdam). 45(4):395-396, 1977.

The acute and subacute effects of the dipivaloyl ester of apomorphine (ADPE) on stereotyped behavior and striatal homovanillic acid (HVA) levels are compared. The results show that after repeated treatment with ADPE, tolerance developed to stereotyped behavior and to decrease in striatal HVA levels. It is considered unlikely that this tolerance is due to enzymatic induction since the concentrations of apomorphine in whole brain were found to be similar 2 hours after acute or subacute treatment. It is suggested that this tolerance reflects a subsensitivity of striatal dopamine receptors. 5 references.

001498 Worsham, Elizabeth D.; Freed, Earl X. Center of Alcohol Studies, Rutgers University, New Brunswick, NJ **Dose-response effects of alcohol upon rat strains bred for differences in reactivity to alcohol.** Pharmacology Biochemistry and Behavior. 7(5):421-424, 1977.

To examine dose/response effects of alcohol upon differentially reactive rat strains, two rat strains, designated least and most affected (LA, MA), selectively bred for differential impairment of motor activity following an injection of alcohol, were tested in stabilimeters and compared over a range of ethanol doses. As expected, increasing doses of ethanol produced progressively greater activity decrements in both strains; however, the same dose of ethanol induced a more pronounced decrement in the MA strain than in LA strain at all doses. At the highest alcohol dose (2.25g/kg), the LA animals were twice as active as were the MA strain at the 1.5g/kg dose. This strain difference in impairment was evident within 3 min postinjection and remained throughout the 30 min test session. The results are discussed in terms of differential

neural and behavioral tolerance to ethanol in the two strains. 17 references. (Author abstract modified)

001499 Wurster, Richard M.; Griffiths, Roland R.; Findley, Jack D.; Brady, Joseph V. Dept. of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Reduction of heroin self-administration in baboons by manipulation of behavioral and pharmacological conditions.** Pharmacology Biochemistry & Behavior. 7(6):519-528, 1977.

To determine the efficacy of two procedures to reduce heroin self-administration in baboons, two male baboons responded on a discrete trial choice task in which the animal chose between several mutually exclusive options, one of which was always associated with intravenous infusion of a unit dose of heroin. Experiment I used methods analogous to clinical situations involving opioid maintenance and subsequent detoxification. During initial baseline conditions, baboons consistently preferred an option of heroin and food over an option of saline and food. Selection of heroin was almost entirely eliminated when there was a mutually exclusive choice between heroin and food and chronic noncontingent morphine was administered. Decreasing the dose of noncontingent morphine produced an increased selection of heroin. In Experiment 2, initial baseline conditions were similar to Experiment 1. Food availability was subsequently made contingent upon selection of options involving progressively lower doses of contingent heroin. These manipulations reduced heroin intake to about 15% of baseline levels. The experiments are seen to demonstrate the utility of animal models for studying procedures for the reduction of opiate self-administration. 36 references. (Author abstract modified)

001500 Yeudall, Lorne T.; Walley, Roc E. Alberta Hospital, Edmonton, Alberta T6G 2E9, Canada **Methyphenidate, amygdalectomy and active avoidance performance in the rat.** Journal of Comparative and Physiological Psychology. 91(6):1207-1219, 1977.

To examine the effects of methylphenidate and amygdalectomy on active avoidance performance, amygdalectomized and control rats were given 400 active avoidance training trials in a shuttlebox. Control animals received 0, 4, 8 or 16mg/kg of methylphenidate throughout acquisition; amygdalectomized animals were given the first 200 trials without drug, followed by 200 trials with drug. The administration of methylphenidate produced an abrupt and large improvement in performance in the amygdalectomized animals. One month after acquisition under the drug, retraining without drug revealed a significant retention effect for the three amygdaloid drug groups relative to the nondrug amygdaloid group. These results indicate that although amygdalectomy impairs the performance of avoidance responses, it does not prevent the learning or retention of such responses. Since methylphenidate appears to act primarily on dopaminergic mechanisms, the possible influence of amygdalectomy on such mechanisms is discussed. 26 references. (Author abstract modified)

001501 Zabik, Joseph E.; Lambert, Carol S.; Braude, Monique C.; Maickel, Roger P. Section on Pharmacology, Medical Science Program, Indiana University School of Medicine, Bloomington, IN 47401 **Drug interactions as measured by deprivation-induced fluid consumption.** Pharmacologist. 19(2):175, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of various psychotherapeutic agents, alone or in combination, on deprivation induced fluid consumption in rats was reported. Narcotic agonists had a hyperdipsic effect in single doses; however, a degree of tolerance to this effect occurred with repetitive daily dosages. Cessation of narcotic agonist administration produced a withdrawal response in fluid consumption. Narcotic antagonists caused a reduction in deprivation induced fluid consumption. Repetitive doses did not produce tolerance; on cessation of administration the animals reverted to baseline consumption. Crosstolerance was produced when methadone was administered to animals repetitively dosed with alpha-acetylmethadol or vice versa. In rats dosed repetitively with methadone or alpha-acetylmethadol: 1) single doses of chlordiazepoxide or barbital produced the usual hyperdipsic effect; 2) single doses of naloxone caused an increased hypodipsic effect; 3) the hypodipsic effect of chlorpromazine was unchanged; and 4) the hypodipsic effect of desipramine was significantly antagonized. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

001502 Abernathy, Charles O.; Lukacs, Lorinc; Zimmerman, Hyman J. Liver Research Unit, VA Hospital, 50 Irving Street, N.W., Washington, DC 20422 **Adverse effects of chlorpromazine metabolites on isolated hepatocytes.** Proceedings of the Society for Experimental Biology and Medicine. 155(4):474-478, 1977.

The effects of chlorpromazine (CPZ) and its metabolites in an in vitro model system which assessed whether their effects on isolated rat hepatocytes correlate with their reported in vivo effects are described. Cytotoxicity was measured by the efflux of aspartate aminotransferase to the surrounding medium. Exposure of liver cells to CPZ led to enzyme leakage. The dimethylated metabolites, mono-CPZ and didesmethyl-CPZ, were three and six times, respectively, more potent than CPZ. Hydroxylation of the tricyclic ring at the 7 or 8 position gives rise to compounds that were slightly less active than CPZ, while oxidation of the sulfur atom resulted in inactive analogs. 27 references. (Author abstract modified)

001503 Asbach, H. W.; Holz, F.; Mohring, K.; Schuler, H. W. Department of Urology, Heidelberg University Medical School, Heidelberg, Germany **Lipid haemodialysis versus charcoal haemoperfusion in imipramine poisoning. An in-vitro and in-vivo study.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):69-70, 1977.

In a summary of a paper presented at the 7th International Congress of the European Association of Poison Control Centres, held at Oslo, Norway during June 1976, the relative merits of lipid hemodialysis and charcoal hemoperfusion in imipramine poisoning are evaluated in both in vivo studies in rabbits and in vitro studies. Results indicate the incorporated imipramine is accessible to both lipid hemodialysis and hemoperfusion. Charcoal hemoperfusion eliminated 99% of imipramine from whole blood during 3 hours at an initial imipramine blood concentration of 2mg/ml. In comparison, lipid hemodialysis using soybean oil as dialysate eliminated between 80% and 93% of imipramine from whole blood. 2 references. (Author abstract modified)

001504 Consroe, Paul; Jones, Byron; Martin, Parthena. Department of Pharmacology and Toxicology, College of Pharmacy, University of Arizona, Tuscon, AZ 85721 **Lysergic acid diethylamide antagonism by chlorpromazine, haloperidol, diazepam, and pentobarbital in the rabbit.** Toxicology and Applied Pharmacology. 42(1):45-54, 1977.

The single and interactive iv effects of lysergic acid diethylamide (LSD, 50mcg/kg) given 20 min preceding or following chlorpromazine (CPZ, 1 and 2mg/kg), haloperidol (HPD, 1 and 2mg/kg), diazepam (Diaz, 1 and 2mg/kg), or pentobarbital (Pb, 5 and 10mg/kg) were assessed on electroencephalographic (EEG) cortical voltage output (CVO), behavior, and body temperature in unrestrained rabbits. Depending on dose and administration order, each drug partially antagonized the decrease of CVO and (except for CPZ) the increase in standing duration and frozen like postures caused by LSD. LSD induced hyperthermia was partially antagonized by CPZ and Diaz, not altered by Pb, and augmented by HPD. Novel stereotypy emerged from the interaction of LSD with HPD, Diaz, or Pb. Additionally, three of five rabbits given LSD died shortly after HPD administration. These data indicate that LSD is partially but not completely antagonized by these drugs, and the nature of the interaction with LSD depends on dose and order of LSD/drug administration. 33 references. (Author abstract)

001505 Elo, Heikki; Ylitalo, Pauli. Dept. of Biomedical Sciences, University of Tampere, Box 607, SF-33101 Tampere 10, Finland **Substantial increase in the levels of chlorophenoxyacetic acids in the CNS of rats as a result of severe intoxication.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(3):280-284, 1977.

In a letter to the editor, the levels of chlorophenoxyacetic acids in the central nervous system of rats brought about by poisoning with these compounds were investigated. Chlorophenoxyacetic acids are used as herbicides and their toxic mechanisms are unclear. The results indicated that during acute poisoning with these compounds their levels in the brain are substantially increased. This increase is closely associated with toxic symptoms and indicates the central nervous system as a target organ in the toxicity of the compounds. 10 references.

001506 Ezrin-Waters, Cheryl; Seeman, Philip. Department of Pharmacology, Medical Sciences Building, University of Toronto, Toronto, Ontario M5S 1A8, Canada **Tolerance to haloperidol catalepsy.** European Journal of Pharmacology (Amsterdam). 41(3):321-327, 1977.

Development of tolerance to the extrapyramidal symptom of catalepsy was studied in male Wistar rats. Catalepsy was measured by placing the front paws of the rat on a horizontal bar suspended 10 cm above a platform. The maximal allowable duration for each trial was 60 sec, and there were two trials. The rats were given 1, 2, or 4mg/kg orally or 0.5, 1, or 2mg/kg i.p. haloperidol and tested for catalepsy each hr for 4 hr. Then for 16 days, the rats were given haloperidol orally, and on the 17th day, they were again tested for catalepsy. All animals became tolerant to the cataleptogenic action of haloperidol. In another experiment, in which animals were monitored each day for cataleptic tolerance for 16 days, haloperidol tolerance developed in two phases, the rapid phase having a half-time of 2.5days and the slow phase a half-time of 5.5days. The intensity of catalepsy in tolerant animals returned to normal after an additional 16 days abstinence from haloperidol. 33 references.

001507 Gough, A. L.; Olley, J. E. School of Pharmacology, University of Bradford, Bradford BD7 1DP, England **Delta9-tetrahydrocannabinol and the extrapyramidal system.** Psychopharmacology (Berlin). 54(1):87-99, 1977.

The behavioral effects of stereotypy and catalepsy by delta9-tetrahydrocannabinol (delta9-THC) in the rat were estimated and the possible involvement of the basal ganglia in these behaviors was studied using brain lesion techniques. In addition, the interactions of delta9-THC with a dopaminergic (amphetamine) and a cholinergic stimulant (RS-86) were evaluated. The excitatory effects of delta9-THC alone, i.e. circling, sniffing, and head movements, were of low intensity and short duration and they were not significantly affected by lesions in the basal ganglia. On the other hand, delta9-THC was found to depress behavior, including catalepsy and atonic muscular prostration, the former being markedly potentiated, while prostration was unaffected by such lesions. Delta9-THC was also found to potentiate cholinergic induced catalepsy, extrapyramidal lesions causing further potentiation. It is suggested that delta9-THC exerts its cataleptogenic and some of its amphetamine interaction effects by reducing dopaminergic transmission in the basal ganglia. 41 references. (Author abstract modified)

001508 Harvey, John A.; McMaster, Scott E. Dept. of Psychology, University of Iowa, Iowa City, IA 52242 **Fenfluramine: cumulative neurotoxicity after chronic treatment with low dosages in the rat.** Communications in Psychopharmacology. 1(1):3-17, 1977.

The cumulative neurotic effects of chronic treatment with low dosages of fenfluramine were studied in rats. A single intraperitoneal injection of fenfluramine hydrochloride at dosages of 12.5to 100micromol/kg produced detectable signs of neurotoxicity in cresyl violet stained sections consisting of an intense staining of cell bodies, an irregular and shrunken appearance of the cells and a perineuronal space. This cytotoxic reaction was consistently observed in the B-9 serotonergic cell group and was dose dependent. The neurotoxic action of fenfluramine was paralleled by a dose dependent decrease in brain content of serotonin. Ten daily injections of 12.5micromol/kg fenfluramine produced a greater neurotoxic and serotonin depleting effect than a single dose of 25micromol/kg. There was no evidence of serotonin depletion or neurotoxicity after 10 daily injections of 6.25micromol/kg. The dosage of 12.5micromol/kg is within the human dose range suggesting a possible neurotoxic hazard of chronic fenfluramine treatment in man. 15 references. (Author abstract modified)

001509 Honma, T.; Fukushima, H. Research and Development Ctr., Pharmaceuticals Div., Sumitomo Chemical Co., Ltd., 2-1, 4-Chome, Takatsukasa, Hyogo 665, Japan **Role of brain norepinephrine in neuroleptic-induced catalepsy in rats.** Pharmacology Biochemistry & Behavior. 7(6):501-506, 1977.

The role of brain norepinephrine (NE) and striatal dopamine (DA) in neuroleptic induced catalepsy in rats was studied in an attempt to determine the mechanism of action in extrapyramidal side-effects elicited by neuroleptics in humans. Bis (4-methyl-1-homopiperazinylthiocarbonyl) disulfide (FLA-63) and diethyldithiocarbamate enhanced the catalepsy induced by haloperidol in rats. The NE content of the diencephalon in rats treated with haloperidol and FLA-63 was less than that in rats treated with haloperidol alone. The DA decrease in the striatum of haloperidol treated rats was not altered by FLA-63. Intraperitoneally or intraventricularly administered phentolamine enhanced the catalepsy induced by heloperidol, and clonidine counteracted this effect; propranolol failed to change haloperidol induced catalepsy. FLA-63 enhanced the catalepsy induced by ID-4708 (a new butyrophenone compound) by an extent greater than that caused by haloperidol. ID-4708 was more potent in increasing the NE turnover than haloperidol. The combined administration of ID-4708 and FLA-63 produced a greater decrease in the NE content than the combination of

haloperidol and FLA-63. These results suggest that the neuroleptic induced capalepsy would be facilitated when the activity of the NE neurons is lowered or when alpha receptors are blocked. A decrease in the activity of DA neurons or the blockade of the DA receptors is essential to elicit catalepsy in rats, and the function of NE neurons would play a role in regulating the degree of catalepsy. 30 references. (Author abstract modified)

001510 Krebs, Steven J.; Abbatiello, Elvera R. St. John's University College of Pharmacy, Jamaica, NY 11439 **The developmental effects of morphine sulfate and naloxone hydrochloride in the rat.** Pharmacologist. 19(2):179, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of morphine sulfate and naloxone hydrochloride on fetal development after administration to pregnant rats selected periods of gestation was reported. Morphine was administered from days 8 to 17 at an initial dose of 10mg/kg every 12 hr. This dose was increased by increments of 10mg/kg daily. Naloxone was administered in a low dose regimen or in a high dose regimen. At sacrifice on day 20 of gestation, the fetuses were examined. A kidney anomaly was found in 22.4% of the fetuses from the low dose naloxone group and in 2.1% of the fetuses from the high dose naloxone group. Mean weight differences were also found between control and naloxone treated fetuses. (Author abstract modified)

001511 Leander, J. D.; Lucot, J. B. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Toxic interactions of stimulants, narcotics and narcotic antagonists.** Research Communications in Chemical Pathology and Pharmacology. 17(2):255-264, 1977.

The lethality of combinations of central nervous system stimulants, narcotics, and narcotic antagonists was examined in rodents housed individually. The lethality of mice and rats from d-amphetamine was potentiated by methadone, cyclazocine, and morphine, in that order of potency. Naloxone did not enhance lethality from d-amphetamine in mice, whereas it did antagonize lethality from morphine-d-amphetamine interactions. Naloxone did slightly enhance lethality from d-amphetamine in rats, but at a higher dose than those found to antagonize the lethality from morphine-d-amphetamine combinations. Methadone also enhanced the lethality from cocaine. Results were discussed as implications for drug abusers and for patients being treated for narcotic addiction with either a methadone maintenance program or a cyclazocine administration program. 17 references. (Author abstract modified)

001512 Lewis, P. D.; Patel, A. J.; Bendek, G.; Balazs, R. Department of Histopathology, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS, England **Do drugs acting on the nervous system affect cell proliferation in the developing brain?** Lancet (London). No. 8008:399-401, 1977.

The possibility that drugs which affect neurotransmitter activity may, while failing to cause gross structural malformations of the brain, produce long-lasting functional disturbances when given to the developing brain was studied in neonatal rats. Reserpine interfered with cell proliferation in the brain of the neonatal rat and depressed in vivo DNA synthesis when given in a dose of 0.1to 2.5mg/kg, with differential effects within various brain regions. It is theorized that neurotransmitters may act as hormones controlling cell replication in the brain; therefore, drugs which affect neurotransmitter balance could disturb the production of cells. It is suggested that drugs influencing central neurotransmitter activity, such as phenothiazines and adrenergic agonists and antagonists, which in clinical practice are often given to pregnant mothers, may affect the developing brain through mechanisms similar to these reported for reserpine. 21 references.

001513 Lyubimov, B. I.; Yavorskiy, A. N.; Goryanov, O. A.; Rychko, A. V.; Samoylov, N. N. Laboratoriya obshchey farmakologii, Institut Farmakologii AMN SSSR, Moscow, USSR **/Pathogenesis of lithium induced polyuria./** O patogeneze litievoy poliurii. Farmakologiya i Toksikologiya (Moskva). 40(1):76-79, 1977.

Based on previous reports that therapy of affective states with lithium salts led to polyuria, an attempt was made to define its pathogenesis. Experiments conducted with 54 male rats showed that diurnal changes in the neurosecretion of the supraoptic nuclei and of the neurohypophysis in the course of i.p. administration of LiCl over a period of 6 days paralleled histochemical changes in renal acid mucopolysaccharides, corresponding to the nature of disuretic disorders. By the fifth day LiCl interfered with the antidiuretic effect of a single subcutaneous injection of pituitrin. It is inferred that LiCl polyuria is caused by a disorder in synthesis and secretion of diuretic hormone, and by the ability of lithium to mitigate the renal action of this hormone. 12 references. (Journal abstract modified)

001514 Martin, James R.; Novin, Donald. Department of Psychology, UCLA, Los Angeles, CA 90024 **Decreased feeding in rats following hepatic-portal infusion of glucagon.** Physiology & Behavior. 19(4):461-466, 1977.

To further investigate the role of pancreatic glucagon in controlling food intake, male rats received a single hepatic portal injection following mild food deprivation. Cumulative food intake measured after 1/2 hr through 20 hr was decreased by the hormone. The absence of a concomitant decrease in water intake suggested a specific effect of glucagon on feeding, and this specificity was further demonstrated by an hepatic portal infusion of the hormone as the unconditioned stimulus for the formation of a conditioned taste aversion, which did not produce avoidance of a novel taste. Pairing the taste with an intraperitoneal injection of lithium chloride produced a learned taste aversion. It was concluded that the decreased feeding following infusion of a low concentration of pancreatic glucagon through a chronic hepatic portal cannula cannot be attributed to visceral malaise. The relatively specific effect of glucagon on short-term feeding probably results from activation of hepatic glycogenolysis, with the long-term effect possibly due to gluconeogenesis. 29 references. (Author abstract modified)

001515 Martz, Fred; Failinger, Conrad, III; Blake, David A. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Phenytoin teratogenesis: correlation between embryopathic effect and covalent binding of putative arene oxide metabolite in gestational tissue.** Journal of Pharmacology and Experimental Therapeutics. 203(1):231-239, 1977.

The possibility that phenytoin teratogenesis is due to an arene oxide (epoxide) metabolite was examined in Swiss mice. On gestational day 11, pregnant mice were given teratogenic doses of phenytoin with and without a nonteratogenic dose of 1,2-epoxy-3,3,3-trichloropropane (TCPO), an epoxide hydratase inhibitor. TCPO significantly increased the incidence of phenytoin induced cleft lip and palate and enhanced the

embryolethality twofold over phenytoin alone. After treatment with radiolabeled phenytoin, the covalent binding of phenytoin radioactivity in fetuses and placentae was doubled in groups cotreated with TCPO. TCPO did not alter malternal plasma levels of phenytoin or fetal and placental phenytoin uptake. It is postulated that phenytoin teratogenesis results from phenytoin epoxide formation and the covalent binding of the epoxide, the ultimate teratogen, to constituents of gestational tissue. 26 references. (Author abstract modified)

001516 Osgood, Patricia F.; Howes, John F. Sisa Incorporated, 767B Concord Avenue, Cambridge, MA **Delta9-tetrahydrocannabinol and dimethylheptylpyran induced tachycardia in the conscious rat.** Life Sciences (Oxford). 21(9):1329-1335, 1977.

A procedure is reported whereby i.p. doses of delta9-tetrahydrocannabinol and dimethylheptylpyran induced tachycardia in the conscious rat. Since cannabinoids lead to dose related tachycardia in man but dose dependent bradycardia has been reported thus far in laboratory animals, there would seem to be a need for an experimental model in which the effect seen in man (tachycardia) could be reproduced and explored. In the conscious rat, the compounds delta9-tetrahydrocannabinol (THC) and dimethylheptylpyran (DMHP) injected i.p. led to dose related increases in heartrate at 10 to 20 minutes after administration. In vehicle (ethanol) control rats there were small increases in heartrate. Propranolol given before THC resulted in a parallel shift to the right of the dose/effect curve. Adrenalectomy led to a significant decrease in tachycardia following THC and DMHP while ganglionic block markedly decreased the heartrate increases after delta9-THC. Systolic blood pressure at nearly all doses of delta9-THC was minimally affected, although it tended to decrease with increasing dose. Tachycardia in the rat may be the result of a centrally medicated release of epinephrine from the adrenal gland. 26 references. (Author abstract modified)

001517 Petersen, Kurt Pfeiffer. DAK Laboratories, 59, Lergravsvej, DK-2300 Copenhagen, S, Denmark **Effect of age and route of administration on LD50 of Litium chloride in the rat.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):69, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the effect of age and route of administration on the lethal dose 50 (LD50) of lithium chloride (Li) was studied in the rat. LD50 in 3-week-old and 6-week-old rats after oral administration (Or) was significantly higher than LD50 after intraperitoneal (ip) or subcutaneous administration (sc). This difference was not found in 3-month-old and 6-month-old rats. LD50 after Or in 6-week-old rats was higher than for the other ages and this difference was significant for 3-month-old and 6-month-old rats. It was concluded that age and route of administration are of importance for LD50 of Li in the rat.

001518 Puisto, E.-L.; Mattila, M. J. Department of Pharmacology, University of Helsinki, Helsinki, Finland **Prostaglandins and the cardiotoxic effect of doxepin in rabbits and guinea-pigs.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):70, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the effects of prostaglandins (PG) on the cardiotoxic effect of doxepin in rabbits and three tricyclic antidepressants (TCA) in guinea pigs were studied to evaluate the role of PG in the dysrrhythmias provoked by TCA in conscious rabbits. Pretreatment with indomethacin, aminophenazone, or tophenamic acid did not modify the doses of doxepin needed to provoke dysrrhythmias in conscious rabbits. PGF2a elevated blood pressure and somewhat protected rabbits against the lethal effect of doxepin. In conscious or urethane anesthetized guinea pigs the doses of protriptyline were twofold those of doxepin or amitriptyline needed to provoke electrocardiograph changes, suggesting that the TCA carciotoxicity in guinea pigs is about similar to that of rabbits. PGF2a given prior to or simultaneously with doxepin lowered the arrhythmogenic dose of doxepin thus enhancing its toxicity. It was concluded that due to species differences in this respect the therapeutic aspects with PG in dysrrhythmias may prove complicated.

001519 Sangster, B.; Van Heijst, A. N. P.; Zimmerman, A. N. E.; De Vries, H. W. National Poison Information Centre, National Institute of Public Health, Bilthoven, The Netherlands **Intoxication by orphenadrine HCL; mechanism and therapy.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):129-136, 1977.

At the 7th International Conference of the European Association of Poison Control Centres held in Oslo, Norway during June 1976, the pathophysiology of intoxication by orphenadrine is discussed following a review of 158 overdose cases and laboratory studies using five anesthetized, intact dogs. The studies were conducted because of the low lethal dosage, fast course of intoxication, and failure of therapy in orphenadrine overdose. Experimental monitoring of aortic pressure during administration of lethal dose, sublethal dose and a counteracting dose of droperidol is reported. The results indicated that orphenadrine, which in overdose cases produced coma with or without hypoventilation, shock and cardiac arrhythmias, proved to be a cardiotoxic drug when administered in overdose to dogs, and fatal within 90 min. Its cardiotoxic influence appeared to be conteracted by the administration of droperidol, even when administered 40 min after ingestion of orphenadrine tablets.

001520 Siegel, P.; Siegel, M. I.; Krimmer, E. C.; Doyle, W. J.; Barry, H., III. Anthropology Department, Faculty of Arts and Sciences, University of Pittsburgh, Pittsburgh, PA 15260 **Fluctuating dental asymmetry as an indicator of the stressful prenatal effects of delta9-tetrahydrocannabinol in the laboratory rat.** Toxicology and Applied Pharmacology. 42(2):339-344, 1977.

To examine the prenatal effects of delta9-tetrahydrocannabinol (THC) administration on offspring, using fluctuations of dental asymmetry in pups as an indicator of stressful effects, groups of pregnant laboratory rats were given oral doses of THC (5 or 20mg/kg) or its vehicle (propyleneglycol) and additional nondosed groups were pair fed with the high dose group or were allowed continuous access to food. A previously tested technique was used to assess the stressful effects on the offspring. Increased fluctuating dental asymmetry was found in the mandibular dentition of the offspring of THC treated animals. As the experimental design was controlled for route of administration, drug vehicle, and drug induced dietary variation, it is concluded that THC was stressful. An alternative to placental transfer, behavioral stress is a possible explanation for this effect. 18 references. (Author abstract modified)

001521 Stolyarchuk, A. A.; Umanets, V. S. Kafedra farmakologii, Vinnitskiy meditsinskiy institut im. N. I. Pirogova, Vinnitsa, USSR **Effect of lithium chloride on certain indices of cardiac function./** Vliyanie litiya khorida na nekotorye

pokazateli funktsii serdtsa. Farmakologiya i Toksikologiya (Moskva). 40(1):33c36, 1977.

Based on earlier reports of toxic properties of lithium chloride, widely used in Soviet psychiatry, a study was made of the effects of 100mg/kg LiCl on EEG in cats, rats, and rabbits. LiCl was found to increase the voltage of P-waves and R-waves, increase the S-T interval, and slow the rhythm of cardiac contractions. In doses of 50 to 300mg/kg LiCl increased coronary circulation in narcotized cats. 11 references. (Journal abstract modified)

001522 Szukalski, B.; Kobylinska, M. Dept. of Drugs Metabolism, Institute of Pharmaceutical Industry, ul. Rydygiera 8, 01-793 Warsaw, Poland **Effects of IFC-45, a new benzonaphtyridone derivative with antidepressive action, on activity of the rat suprarenal gland cortex.** International Pharmaceutical Abstracts. 14(17):932, 1977.

The toxic effects of 10-dimethylaminopropyl-7-chlorobenzo-(b)-(1,8)-naphthyrid-5-one (IFC-45), a new benzonaphtyridone derivative with antidepressant activity, on the rat suprarenal gland cortex are reported. Daily subcutaneous administration of IFC-45 in doses one tenth of the LD 50 induced hypertrophy of the rat suprarenal gland, especially in females, within 1 month. Within the first 7 days of treatment, blood corticosterone levels increased. After 1 month, blood corticosterone levels fell below the normal level, although no distinct changes in the corticosterone content of the suprarenal gland were noted. A possible mechanism of action of IFC-45 on the rat suprarenal gland cortex is discussed. 14 references. (Author abstract modified)

001523 Van Thiel, David H.; Williams, William D., Jr.; Gavaler, Judith S.; Little, Joanna M.; Estes, Larry W.; Rabin, Bruce S. 1000G Scaife Hall, Division of Gastroenterology, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Ethanol -- its nephrotoxic effect in the rat.** American Journal of Pathology. 89(1):67-84, 1977.

The nephrotoxic effect of ethanol feeding on renal structure and function was evaluated in rats and compared to that in dextrose fed isocaloric control animals. Alcohol fed animals had larger kidneys than their controls. Despite this increase in renal mass, the alcohol fed animals had a 50% reduction in creatinine clearance and a 67% reduction in osmolar clearance compared to their controls. When specific renal constitutents were compared, the alcohol fed animals were found to have twice the renal protein and a 50% increase in renal lipid. Despite these marked structural and functional differences, the light microscopic appearnce of the kidneys of the two groups did not appear significantly different. In contrast, the electron microscopic differences were substantial. The renal epithelial cells, particularly of the distal tubules and Henle's loops, were found to show varying degrees of cellular injury and were observed to be sloughing into the lumens. These electron microscopic observations are similar to those obtained in tubular necrosis due to a variety of nephrotoxic agents. Chronic alcohol feeding of rats produces significant renal dysfunction and adnormalities of structure such that ethanol should be considered a true nephrotoxin. 40 references. (Author abstract)

001524 Weinberg, Andrew D.; Dimen, Edward M.; Simon, Glenn Stuart; Harris, Louis S.; Borzelleca, Joseph F. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Measurements of weight and activity in male mice following inhalation of cannabis smoke in a controlled smoke exposure chamber.** Toxicology and Applied Pharmacology. 42(2):301-307, 1977.

A controlled smoke exposure chamber for delivering cannabis smoke to mice is described, and two studies employing this device, assessing the effects of exposure to marihuana smoke on weight and activity in mice, are reported. Standardized smoking conditions were achieved with this unit yielding a concentration of 0.123mg/liter of delta9-tetrahydrocannabinol in air. A significant decrease in locomotor activity in treated animals was seen following the fourth treatment in a 21 day study where animals were exposed three times weekly for 3 weeks. A significant decrease in bodyweight for marihuana exposed animals was also noted. In another study, animals were exposed daily for 7 days. Locomotor activity was significantly decreased in marihuana exposed animals on days 6 and 7. There was no significant change in bodyweight. Following removal from the exposure chamber, the marihuana exposed animals showed transient hyperactivity (1 to 3 min) followed by a period of depressed activity lasting 1 hour. Some tolerance to the placebo smoke was seen after the fourth treatment in both studies. Cumulative effects were seen following repeated exposures. These preliminary data suggest that inhalation of marihuana smoke will initiate behavior changes in mice. 10 references. (Author abstract modified)

001525 Yavorskiy, A. N.; Samoylov, N. N.; Rychko, A. V. Laboratoriya obshchey farmakologii, Institut farmakologii AMN SSSR, Moscow, USSR /**Effect of lithium chloride on the neurosecretory system of the rat hypothalamus.**/ Vliyaniye khlorida litiya na neyro-sekretornuyu sistemu gipotalamusa krys. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 83(1):32-34, 1977.

Cytochemical analysis was made of the reaction of the hypothalamo/hypophyseal neurosecretory system to administration of lithium chloride. The reaction of this system proved to depend directly on the amount of lithium administered and was characterized by activation of synthesis, and elimination of the neurosecretion with a single administration, or depression of hormonopoiesis in the hypothalamus and exhaustion of stores of neurosecretion in the neurohypophysis during continued application. During the restoration period, or 7 to 30 days after stopping the drug administration, the state of the hypothalamo/hypophyseal neurosecretory system gradually returned to normal. It is concluded that changes in the central mechanisms of neuroendocrine regulation at the hypothalamic level which are caused by the lithium were significant in the pathogenesis of side-effects of its salts. 12 references. (Journal abstract modified)

06 METHODS DEVELOPMENT

001526 Bunney, Benjamin S. Departments of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Central dopaminergic systems: two in vivo electrophysiological models for predicting therapeutic efficacy and neurological side effects of putative antipsychotic drugs.** In: Hanin I., Animal models in psychiatry and neurology. Oxford, Pergamon, 1977. (p. 91-105).

Two in vivo animal research models which use drug induced changes of central dopamine (DA) containing and DA innervated neurons, respectively, to predict therapeutic and adverse neurological effects of putative antipsychotic drugs are presented. In the first model specific changes in the firing rate of DA neurons appear to correlate with the clinical actions of known neuroleptics: 1) antipsychotic drug effects are associated with the reversal of amphetamine induced depression of DA containing neurons in the midbrain ventral tegmental

area; and 2) drugs with a moderate to high incidence of extrapyramidal sideeffects increase the activity of substantia nigra zona compacta dopaminergic neurons above baseline levels, and reverse d-ampheetamine induced depression in these cells to above baseline levels. In the second model, drug induced changes in the ability of mircroiontiophoretic DA to depress activity in neurons receiving DA innervation appear to correlate with the clinical effects of known neuroleptics. 49 references.

001527 Dahlstrom, Bengt; Paalzow, Lennart; Edlund, Per Olov. Dept. of Pharmacology, University of Uppsala, Biomedical Center, Box 573, S-75123 Uppsala, Sweden **Simultaneous determination of codeine and morphine in biological samples by gas chromatography with electron capture detection.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(3):273-279, 1977.

A sensitive gas chromatographic method for the simultaneous determination of codeine and morphine in plasma and brain samples is described. The method involves solvent extraction of the compounds from plasma, derivatization with pentafluoropropionic anhydride and subsequent separation on a 3% OV-17 column. The quantification is performed with electron capture detection. The sensitivity of the method makes it especially useful for pharmacokinetic investigations. The method was successfully applied to determine the time course of codeine and its metabolite morphine after intravenous administration of codeine to the rat. 9 references. (Journal abstract)

001528 Grove, Robert N.; Verreault, Richard. Dept. de Pharmacologie, Universite Laval, Quebec, P.Q. G1K 7P4, Canada **Intravenous cocaine self-administration in the rabbit.** Progress in Neuro-Psychopharmacology. 1(3/4):347-350, 1977.

The rabbit is described as an experimental subject for use in infrahuman intravenous drug self-administration research, and a new method for inducing cocaine self-administration in the rabbit is offered. An operant conditioning chamber was developed which permits intravenous infusions contingent upon barpressing in semirestrained catheterized rabbits. Results of experiments indicate short-term regular patterning of cocaine infusions. It is concluded that cocaine reinforced operant behavior in the rabbit is similar to that for rats and monkeys, and that the rabbit may be an excellent subject for selected studies in drug self-administration. 10 references.

001529 Huberman, Harris S.; Eison, Michael S.; Bryan, Karen Smith; Ellison, Gaylard. Department of Psychology, UCLA, 405 Hilgard Avenue, Los Angeles, CA 90024 **A slow-release silicone pellet for chronic amphetamine administration.** European Journal of Pharmacology (Amsterdam). 45(3):237-242, 1977.

A slow release amphetamine pellet consisting of a silicone capsule containing dextroamphetamine base in polyethylene glycol is described. When implanted subcutaneously in rats this pellet produces brain levels of drug initially comparable to an intraperitoneal dose of 2mg/kg of dextroamphetamine sulfate; these levels gradually fall but appreciable amphetamine remains present in the brain for over 10 days. Studies of the behavioral effects of the drug administered via this pellet have indicated that: 1) rats implanted with the pellets exhibit sustained motor stereotypies and constant hyperactivity in stabilimeters for 2 to 3 days; 2) 4 days after implantation, activity declines to near control levels even though amphetamine is still present in the brain; and 3) during this later stage, rats show exaggerated startle responses and resist handling. It is suggested that the pellet is a unique tool for the study of the behavioral and physiological effects of prolonged amphetamine intoxication. 10 references. (Author abstract modified)

001530 Kier, Lemont B.; Hall, Lowell H. Department of Pharmaceutical Chemistry, Medical College of Virginia, Richmond, VA 23298 **Structure-activity studies on hallucinogenic amphetamines using molecular connectivity.** Journal of Medicinal Chemistry. 20(12):1631-1636, 1977.

A series of 23 ring substituted hallucinogenic amphetamines has been analyzed using molecular connectivity. A correlating equation has been found between potency and connectivity terms. The equation permits an interpretation of structure/activity relationships. The equation is capable of predicting potency for amphetamines not in the list and mescalines and tryptamines. It is concluded that a structural description, using three molecular connectivity indices, results in a good correlation with the hallucinogenic potency of a list of amphetamines. 11 references. (Author abstract modified)

001531 Latham, A. N. McMaster University Medical Centre, Hamilton, Ontario L8S 4J9, Canada **A new chronically cannulated carotid artery preparation for determination of drug half-lives in the guinea pig.** Canadian Journal of Physiology and Pharmacology (Ottawa). 55(4):773-777, 1977.

A reliable procedure for implanting a cannula into the carotid artery of the guinea-pig is described. The gaseous anesthetic used provided excellent control, rapid recovery, and caused no fatalities. There was no evidence of postoperative infection and patency of the cannula could be maintained for 21 days after surgery. There was no indication of post-operative trauma and removal of blood appeared to be painless. Efficacy of the preparation was demonstrated by repeated removal of 3ml blood for the determination of the half-life of phenobarbital acutely in five animals and chronically in three guinea-pigs treated with the drug for 14 days. Administration of phenobarbital twice daily for 1 week increased its clearance rate fivefold. Treatment for an additional week produced a further increase in phenobarbital clearance. The cannulated guinea-pig preparation described should allow determination of the pharmacokinetics of many drugs in this species. 9 references. (Author abstract modified)

001532 Leberer, Mark R.; Fowler, Stephen C. Department of Psychology, Fayetteville State University, Fayetteville, NC 28301 **Drug discrimination and generalization in pigeons.** Pharmacology Biochemistry and Behavior. 7(5):483-486, 1977.

To examine drug discrimination and generalization in the pigeon using a three key operant conditioning procedure, six pigeons were trained to select the response key which was associated with each of three drug treatment conditions: d-amphetamine (2mg/kg), pentobarbital (5mg/kg), and saline. Thus, the drug state served as a discriminative stimulus for food reinforcement. After 20 sessions of discrimination training in each of the three conditions, more than 90% of the responses were correctly emitted in the presence of the appropriate drug or saline stimulus. Acquisition of the discrimination progressed at approximately equal rates for the three treatments. Subsequent to discrimination training, generalization gradients were obtained for several doses of the training drugs and for dose ranges of cocaine, morphine, and methocarbamol. The pigeons responded to morphine by choosing the key paired with pentobarbital during training; further, cocaine administration resulted in choice of the amphetamine key. However, methocarbamol, over the doses used, produced

responding more characteristic of saline than of the other training drugs. The data suggest that a three key operant discrimination procedure using pigeons provides a sensitive method for investigating the stimulus properties of relatively low doses of behaviorally relevant drugs. 18 references. (Author abstract modified)

001533 Ljungberg, T.; Ungerstedt, U. Department of Histology, Karolinska Institutet, Stockholm, Sweden **Different behavioural patterns induced by apomorphine: evidence that the method of administration determines the behavioural response to the drug.** European Journal of Pharmacology (Amsterdam). 46(1):41-50, 1977.

To examine the effects of apomorphine preparation and administration procedures on behavioral response, the behavioral effects of subcutaneously (s.c.)injected apomorphine were studied on habituated rats in a test box designed to measure eight different components of behavior. Apomorphine, 1mg/kg, induced two different behaviors: the G-type of behavior characterized by compulsive gnawing and the LS type of behavior characterized by increased locomotion, sniffing and repetitive head and limb movements. G-type behavior was induced when apomorphine, dissolved by heating, was injected s.c. into the flank of the animal. LS type behavior was induced both when apomorphine, dissolved by heating, was injected s.c. into the neck and when it was dissolved by heating together with a high concentration of ascorbic acid (1mg/ml) and injected s.c. into the flank. G-type behavior could not be elicited by changing the dose which induced LS type behavior or vice versa. It is concluded that these different behavioral effects of apomorphine were not dose/response effects but were elicited by at least two different synaptic mechanisms in the brain. Experimentally induced changes from one of these apomorphine induced behaviors to another can therefore not merely be interpreted as a change in the intensity of the behavioral response as is done in commonly used stereotypy rating scales. 33 references. (Author abstract modified)

001534 Lucek, Rudolph; Dixon, Ross. Research Division, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Specific radioimmunoassay for amitriptyline and nortriptyline in plasma.** Research Communications in Chemical Pathology and Pharmacology. 18(1):125-136, 1977.

A specific radioimmunoassay (RIA) for the determination in plasma of the widely used tricyclic antidepressant amitriptyline (AT) and its major metabolite nortriptyline (NT) has been developed employing (3H)AT as the radioligand and a rabbit antiserum to a bovine serum albumin conjugate of N-succinylnortriptyline. Although the antiserum cross-reacts almost equally well with AT and NT, specificity is achieved by selective extraction of each compound from plasma at a different pH. A unique aspect of the assay is that at no time during the entire extraction procedure is the AT or NT taken out of solution. Both compounds are back extracted from the organic phase into O.lN HCl and the acid fraction subjected to RIA directly. The method has a limit of sensitivity of about 2ng/ml using a O.5ml sample of plasma. Satisfactory agreement was obtained for plasma levels of AT and NT when determined by the RIA and a specific GC/MS procedure. The correlation coefficients were 0.89 and 0.98 for AT and NT, respectively. The RIA has been used to measure steady state levels of AT and NT in man after chronic administration of AT and following a single oral 75mg dose. The method also lends itself for the specific determination of NT alone in subjects receiving therapeutic doses of NT. 21 references. (Author abstract)

001535 Marcy, R.; Quermonne, M. A.; Nammathao, B. Dept. of Pharmacology, Pharmaceutical Sciences Unit, University of Caen, F-14000 Caen, France **Antagonism of skin conductance response (SCR) habituation during iterative photostimulation in mice: habituation test -- a new psychopharmacological method for detecting and quantifying enhancement of psychic activity.** Psychopharmacology (Berlin). 54(1):73-80, 1977.

A method for studying habituation of the palmar skin conductance response during iterative photostimulation in mice is described. Twenty drugs known for their CNS stimulant activity or beneficial action on learning were tested for their antagonism toward habituation. With most of the drugs tested, the delay in skin conductance response extinction was dose dependent. From the corresponding regression equations, the standard delaying doses were computed and used for classification. Locomotor activity tests were run in parallel with habituation tests and the two sets of results compared. Reliability of the habituation test was checked. The responsiveness of the test and the significance of the results are discussed. The applicability of the habituation test in psychopharmacological research is argued by its sensitivity to piracetam, whose nootropic activity is not detectable by classic behavioral methods. 54 references. (Author abstract modified)

001536 Miller, Dean G.; Mallov, Samuel. Dept. of Pharmacology, SUNY, Upstate Medical Center, Syracuse, NY 13210 **Quantitative determination of stress-induced myocardial damage in rats.** Pharmacology Biochemistry & Behavior. 7(2):139-145, 1977.

Several methods for assessing the degree of myocardial damage induced in rats by exposure to unsignalled, irregular footshock stress were evaluated. The methods were: 1) measurement of the enzymes lactate dehydrogenase (LDH), glutamate oxalacetate transaminase, and glutamate pyruvate transaminase released into the circulation; 2) measurement of the rate of release of LDH from isolated perfused hearts into the perfusate; and 3) measurement of the in vivo cardiac uptake of the radioactively labeled agents technetium-99m-stannous pyrophosphate or technetium-99m-methylene diphosphonate. The latter two methods permitted quantitative determination of the degree of myocardial damage produced. It is concluded that determination of cardiac technetium-99m uptake is simple, quantitative, highly sensitive, truly indicative of cardiac damage, and the most suitable method for studies of the effects of physiological stress on the heart. 40 references. (Author abstract modified)

001537 Norton, Stata. Department of Pharmacology, University of Kansas Medical Center, Kansas City, KS 66103 **The study of sequences of motor behavior.** In: Iverson, L., Handbook of Psychopharmacology. New York, Plenum, 1977. V. 7 (p. 83-105).

An overview of observational research methodologies for animal behaviors is presented and the application of behavioral observation principals to psychopharmacological studies is illustrated. The discrete motor act presents the smallest unit for observation; determining sequences of behavior involves the analysis of the flow of motor acts in time. Two major approaches to behavior as a stochastic process are considered: the analysis of behavior sequences as permutations, and the analysis of combinations in a specified length of time. Interval histogram analysis of behavior, and the relationship between duration of acts and frequency of acts are considered. Control of environmental factors, data recording, and interobserver and intraobserver reliability are discussed. Psychopharmacological studies employing continuous recording and time

sampling methods are summarized. Stereotypy is briefly discussed. 25 references.

001538 Oliver, A. P.; Hoffer, B. J.; Wyatt, R. J. Laboratory of Neuropharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The hippocampal slice: a system for studying the pharmacology of seizures and for screening anticonvulsant drugs.** Epilepsia. 18(4):543-548, 1977.

The use of the hippocampal slice (guinea-pig) as an in vitro model for studying the pharmacology of seizures and for screening anticonvulsive drugs (phenytoin, diazepam, phenobarbital, and mesuximide) is reported. Interictal spikes with a configuration similar to that occurring in grand mal epilepsy were generated by the application of penicillin to a hippocampal slice preparation. The effect of anticonvulsant drugs on seizure activity was tested at concentrations comparable to reported clinical serum concentrations. Phenytoin and diazepam were maximally effective at concentrations of 20 micrograms/ml and 3 to 4 micrograms/ml, respectively, in good agreement with their effective concentrations in clinical practice. Phenobarbital was more potent (5 micrograms/ml) and mesuximide (50% potent at 80 micrograms/ml) was least effective. 15 references. (Author abstract modified)

001539 Thakkar, Arvind L.; Hirsch, Clarence A.; Page, John G. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Solid dispersion approach for overcoming bioavailability problems due to polymorphism of nabilone, a cannabinoid derivative.** Journal of Pharmacy and Pharmacology (London). 29(12):783-784, 1977.

A solid dispersion approach for overcoming bioavailability problems due to polymorphism of (+/-)-3-(1,1-dimethylheptyl)-6,6abeta,7,8,10aalpha-hexahydro-1-hydrox -6,6-dimethyl-9H-dibenzo (b,d)-pyran-9-one (nabilone), a potentially anxiolytic cannabinoid derivative, is described. An effective way to prevent conversion to the nonbioavailable thermodynamically stable form, involves keeping nabilone dispersed in the water soluble matrix of polyvinylpyrrolidone (PVP) by dissolving nabilone and PVP in 95% ethanol or chloroform followed by removal of the solvent by rotary evaporation and vacuum drying. The dried preparation is then ground and further dried. This dispersion maintains nabilone in a bioavailable form for at least 2 years at room temperature. 5 references.

001540 Tiganov, A. S. Kafedra psikhiatrii, Tsentral'nyy institut usovershenstvovaniya vrachey, Moscow, USSR /**Some problems concerning the techniques of stuying the effectiveness of psychotropic drugs.**/ O nekotorykh voprosakh metodiki izucheniya effektivnosti psikhotropnykh sredstv. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 77(2):269-272, 1977.

Problems concerning the techniques of studying the effectiveness of psychotropic drugs are discussed. Better clinical methods in the identification of symptoms of trial patients with regard to the stage and duration of the particular illness and the consequent effect of psychotropic drugs on similar groups are needed. This would result in a more valid estimation of the effectiveness of different psychotropic preparations. 8 references.

001541 Weeks, James R. Upjohn Company, Kalamazoo, MI 49001 **The pneumatic syringe: a simple apparatus for self-administration of drugs by rats.** Pharmacology Biochemistry & Behavior. 7(6):559-562, 1977.

A pneumatic syringe for the self-administration of drugs by rats is described. A solid state control unit which can operate two syringes (drug injection and flush) is also described. This control unit has outputs for recording responses and injections, and can be programmed to provide several schedules of reinforcement. All components of the apparatus are readily commercially available. Recommended delivery volumes are from 10 to 200 microliters. 6 references. (Author abstract modified)

CLINICAL PSYCOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

001542 Chouinard, Guy; Annable, Lawrence. Research Dept., Hopital Louis-H. Lafontaine, Montreal, Canada **The effect of rubidium in schizophrenia.** Communications in Psychopharmacology. 1(4):373-383, 1977.

A single dose of rubidium chloride was added at each of four dose levels (0.5g, 1g, 1.5g, 2g) to the regular neuroleptic medication of chronic schizophrenic patients in a double-blind, placebo controlled study lasting 56 days. The dose response relationship suggests that rubidium increased the affectivity of these patients. This is consistent with reports of increased activity and alertness induced by rubidium salts in animal studies. The maximum therapeutic effect appeared to occur 3 weeks after ingestion. Further studies are encouraged to determine the value of rubidium in treating schizophrenia, and the proper therapeutic dose range. 14 references. (Author abstract)

001543 Doongaji, D. R.; Sheth, A.; Apte J. S.; Datt, M. R.; Mundra, V. K. Department of Psychiatry, Seth G. S. Medical College, Parel, Bombay 400012, India **Single versus divided doses of Sintamil in depression.** Journal of Postgraduate Medicine (Bombay). 23(3):106-111, 1977.

Fifty one outpatient depressives were treated with Sintamil, a new tricyclic antidepressant belonging to the dibenzoxazepine group. Fifty one outpatient depressives were treated with Sintamil for a 5 week trial period under double-blind conditions. Sintamil 75mg/day was administered in a fixed dosage schedule either as a single daily dose (SDS) or in 3 divided doses (DDS). There were no significant differences between the two treatment modalities in so far as efficacy was concerned. The SDS regiment of drug administration is associated with a lesser incidence of side-effects. 3 references. (Author abstract modified)

001544 Eckert, Elke D.; Zimmermann, Robert; Dehnel, Luther; Schiele, Burtrum C. University of Minnesota Medical School, Minneapolis, MN 55455 **A controlled study of WIN 27,147-2 in the treatment of depression.** Current Therapeutic Research. 22(5, Sect. 1):644-651, 1977.

To determine the efficacy of WIN-27,147-2 (3-(dimethylamino)-1,2,3,4-tetrahydrocorbazole Hcl) in the treatment of depression, 37 depressed male and female patients were treated for four weeks in a placebo controlled double blind study. The WIN-27,147-2 group showed a statistically significant reduction in the anxious depression factor of the Brief Psychiatric Rating Scale and the somatization factor of the Hamilton Depression Scale, plus a greater incidence of drowsiness. The placebo group showed a relatively greater improvement on the retardation scale of the Nurses Observation Scale for Inpatient Evaluation plus a greater incidence of akathisia and restlessness. These findings suggest a drug with antidepressant anxiolytic actions with sedative properties. 5 references. (Author abstract)

001545 Fink, Max; Irwin, Peter; Gastpar, Markus; Deridder, Johannes J. Department of Psychiatry, Health Sciences Center, SUNY at Stony Brook, Stony Brook, NY 11794 **EEG, blood level, and behavioral effects of the antidepressant mianserin (ORG GB-94).** Psychopharmacology (Berlin). 54(3):249-254, 1977.

A pharmacokinetic analysis of a new antidepressant drug, mianserin (ORG GB-94), was undertaken in four male volunteers each of whom received 15mg mianserin on two occasions. Plasma levels peak at 2 h with a median level of 11.0ng/ml, a median beta-phase half-life of 10.0h, and a median apparent volume of distribution of 3.3x1031. EEG profile analysis shows mianserin to increase frequencies below 6Hz, decrease those from 7.5to 15Hz, and increase frequencies above 18Hz, a pattern similar to amitriptyline. Peak EEG effects range from 2 to 5 h with a pattern of measured changes that parallels plasma levels with varying latency. Decreases in vigilance measures and in critical flicker fusion frequency show a similar time course. Mianserin is a putative thymoleptic on EEG profile analysis with high cerebral penetrance. 24 references. (Author abstract)

001546 Frezza, V.; Zantoni, G. Ospedale Psichiatrico Provinciale di Udine, Udine, Italy **/Arginine pyroglutamate (G-278): a clinical experiment./** Il piroglutammato di arginina (G 278): sperimentazione clinica. Rassegna di Studi Psichiatrici (Siena). 66(1):72-82, 1977.

A test was made of arginine pyroglutamate (G-278) with a mixed group of hospitalized mental patients, including schizophrenics, alcoholics, and depressive psychotics. Fifty males, 30 to 70 years old, were divided into two groups and were given two different doses of G-278 or placebo under double-blind conditions. Both groups were treated for 30 consecutive days. Results showed amelioration in almost 63% of cases, and the drug was well tolerated. 19 references.

001547 Halikowski, B.; Piotropawlowska-Weinert, M. Child Neurology Unit, Pediatric Institute, Pommeranian Medical Academy, Szczecin, Poland **Levodopa in subacute sclerosing panencephalitis.** Lancet (London). 2(8046):1033, 1977.

A series of preliminary drug trials undertaken with children in the initial stages of subacute sclerosing panencephalitis (SSPE), characterized by mental perseveration and slowing, speech disorders and ataxic gait, behavior and mood alterations, and hypokinesis, to determine if the inexorable deteriorative course of the disease could be arrested are reported in a letter. Levodopa alone or in combination with carbidopa was administered to 10 children, and 3 children were treated with levodopa, carbadopa, and a monoamine oxidase inhibitor. Four children with Stage 1 SSPE became clinically normal after 1 to 4 weeks treatment as did a child with Stage 2 SSPE. Children in Stages 3 and 4 failed to respond or responded only minimally to treatment. A total of six children have remained free of symptoms following treatment: five for a 3 to 4 month period; and a child initially treated for 2 years. It has been suggested that immunological brain enzyme inhibition and neurone lesion possibly affecting noradrenergic and dopaminergic terminals may explain SSPE; consequently levodopa effects might be overcoming some metabolic block to neurotransmitter synthesis. Further research is recommended. 6 references.

001548 Itil, T. M.; Bhattachyaryya, A.; Polvan, N.; Huque, M.; Menon, G. N. New York Medical College, New York, NY **Fluvoxamine (DU-23,000), a new antidepressant. Quantitative pharmaco-electroencephalography and pilot clinical trials.** Progress in Neuro-Psychopharmacology. 1(3/4):309-322, 1977.

Quantitative pharmaco-EEG studies in healthy volunteers and open pilot trials in depressive hospitalized patients and outpatients with fluvoxamine (DU-23,000) (E)-5-methoxy-4'(trifluoromethyl)valerophone0-(2-aminoethyl)oxime maleate were conducted to determine: 1) the lowest statistically significant effective single dose of fluvoxamine on human brain function as measured by computer EEG changes; 2) whether the EEG profiles of fluvoxamine are similar to those of known antidepressant compounds from a computer data base; 3) establish dose related changes in EEG, thus providing evidence of the pharmacological bioavailability at the CNS level; 4) the CNS responses of the individual Ss, thus providing information on the biological variability of Ss to fluvoxamine; and 5) the therapeutic effects and side-effects of fluvoxamine in depressed hospitalized patients and outpatients. It was found that fluvoxamine, a potent serotonin reuptake inhibitor, has significant effects on human brain function, as measured by computer EEG. Computer EEG profiles resembled those of imipramine in the present study and desimipramine and protriptyline from the computer data base, indicating stimulant antidepressant effects for fluvoxamine. The minimum CNS effective single dose of fluvoxamine was established to be 50mg. On a mg/mg basis, the potency of the CNS effects of fluvoxamine were lesser than those of imipramine. In the open, uncontrolled clinical trials, fluvoxamine showed antidepressant effects in five of 13 patients, therapeutic effects starting with 100mg daily, and as early as 1 week after medication began. Fluvoxamine was effective primarily in symptoms of depressed mood, gastrointestinal symptoms, general somatic symptoms, sexual disturbances, psychic and somatic anxiety, retardation, suicidal thoughts, and hypochondriasis. As major clinical side-effects, insomnia, agitation, restlessness, and increased psychomotor activity were observed. The clinical study is taken to support the quantitative pharmaco-EEG study concerning antidepressant type psychotropic properties of fluvoxamine, some stimulant effects of this compound, and the high biological variablity of Ss to this drug. 13 references. (Author abstract modified)

001549 Jarret, R.; Caille, E.-J.; Bassano, J.-L. Service de Neuro-Psychiatrie, H.I.A.A. Laveran, F-13998 Marseille Armees, France **/Differentiation of hypnotic action of nitrazepam and estazolam and effects on behavior and cortical activity./** Differenciation du Nitrazepam et de l'Estazolam au niveau du processus hypnique, du comportement et de l'electrogenese cerebrale. Psychologie Medicale (Paris). 9(1):153-164, 1977.

A study was made to differentiate between nitrazepam and estazolam in regard to hypnotic action and their effects on behavior and cortical activity. Eight adult volunteers were given nitrazepam, placebo, and estazolam on two consecutive days. Estazolam was found to be significantly more active in effect on sleep induction and in regulation of REM sleep, in effect on behavioral level, and in decreasing the critical frequency of fusion of the EEG. 8 references. (Journal abstract modified)

001550 Jasinski, D. R.; Griffith, J. D.; Pevnick, J. National Institute on Drug Abuse Addiction Research Center, P.O. Box 12390, Lexington, KY 40511 **Nefopam (N), morphine (M), and d-amphetamine (A) in man: subjective, behavioral, and physiologic effects.** Pharmacologist. 19(2):230, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the subjective, behavioral, and physiologic effects of nefopam, an alalgesic with 33% to 50% of the potency of morphine, as compared with those of morphine and amphetamine, was reported. Because animal studies had suggested that nefopam has a profile more like amphetamine than morphine, the study was performed to determine whether nefopam's effects in humans are also more like amphetamine than morphine. Each drug was administered intramuscularly at weekly intervals to nontolerant addicts. Amphetamine and nefopam, but not morphine, increased supine systolic blood pressure and pulse rate. All three drugs increased supine diastolic blood pressure and decreased caloric intake. Only morphine produced miosis; only amphetamine increased body temperature and caused insomnia. No drug changed respiratory rate. Subjects identified nefopam as amphetamine rather than as morphine; however, nefopam and morphine caused sedation, which amphetamine did not. In producing subjective effects, nefopam was one fifth to one tenth as potent as morphine and one third to one fourth as potent as amphetamine. It is suggested that in humans nefopam is more like amphetamine than morphine and that structures not related to amphetamine or cocaine can produce amphetamine-like subjective effects. 2 references. (Author abstract modified)

001551 Klerman, Gerald L. Department of Psychiatry, Harvard Medical School, Boston, MA 02114 **Development of drug therapy for the mentally ill.** Federation Proceedings. 36(10):2352-2355, 1977.

A brief review and evaluation of recommendations of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research pertaining to drug development and research in the fields of mental illness and mental retardation is presented. Treatment and research in the fields of mental illness and retardation have been advanced greatly by the discovery of psychopharmacological agents since the mid-1950's. These agents have improved the care and treatment of individual patients and their availability has stimulated clinical research to evaluate their efficacy, safety, and modes of action and toxicology. Since a significant proportion of the subjects of such research are mentally ill, and institutionalized, special considerations arise as to their protection. Four issues have been generated in the work of the Commission concerning research on drug treatment for the institutionalized mentally ill and mentally retarded. These four issues are: 1) the relevance of biomedical and behavioral research for mental illness in general; 2) justification for the conduct of drug research in institutionalized subjects; 3) the possible limitations of the mentally ill to give truly informed consent; and 4) possible special constraints generated by institutional settings which would limit the conduct and monitoring of drug research. Although the final report of the Commission on these matters has not appeared, the draft documents indicate the Commission is taking a balanced and considered view which proposes the continuation of such research while protecting subjects through strengthening of the Institution Review Boards (IRB), third party consent for subjects found incompetent to provide such consent themselves, and increased responsibility of federal agencies to supervise research in institutional settings. Implications of these recommendations for future conduct of research are discussed. 7 references. (Author abstract modified)

001552 Maltbie, Allan A.; Cavenar, Jesse O., Jr. Psychosomatic and Liaison Service, Veterans Administration Hospital, Durham, NC 27705 **Haloperidol and analgesia: case reports.** Military Medicine. 142(12):946-948, 1977.

Efficacy of haloperidol in a number of disorders is reviewed, and two case reports elucidating the analgesic pro-

perties of haloperidol in four carcinoma patients with and without accompanying psychotic symptomatology are presented. Haloperidol has been used successfully in the treatment of acute and chronic schizophrenia, in the control of hallucinations, in anxiety and mixed neurological states, in obsessive-compulsive disorders, in acute and chronic organic brain syndromes, in delirium tremens and confusional states, in manic psychosis, and Gilles de la Tourette syndrome and Huntington's chorea. Haloperidol has now been found effective as a nonnarcotic analgesic in four terminal carcinoma patients. In two patients the drug relieved hallucinations and delusions as well as pain without additional analgesic medication even during the terminal phase of the illness. In the other cases haloperidol in combination with small quantities of morphine or codeine was found to relieve pain and depressive symptoms. 18 references.

001553 McGeer, P. L.; Brown, W. T.; Zeldowicz, L. Department of Psychiatry, University of British Columbia, Vancouver, Canada **Lack of effect of gamma-hydroxybutyrate in Huntington's chorea.** Canadian Psychiatric Association Journal (Ottawa). 22(2):87-89, 1977.

Observations of an uncontrolled trial of oral gamma-hydroxybutyrate in four cases of Huntington's chorea are reported. All neuroleptics were withdrawn for a week prior to the trial, and gamma-hydroxybutyrate was administered at 1.5g/day and increased to 5.25g/day. The three female patients and one male patient, were 49 to 59 years old, and had a minimum 5 year diagnosis. Mental deterioration was not advanced in any of the patients. Although none of the patients showed objective improvement in motor performance, at lower doses the patients appeared more alert mentally, an elevation of mood was observed, and they exhibited higher motivation to do simple chores independently. No objective explanation is offered for these changes. Brain pathology of one patient who died during the 6th month of therapy is included. 14 references.

001554 Mielke, David H.; Gallant, Donald M.; Kessler, Craig. Dept. of Psychiatry, Tulane Univ. School of Medicine, 1415 Tulane Ave., New Orleans, LA 70112 **An evaluation of a unique new antipsychotic agent, sulpiride: effects on serum prolactin and growth hormone levels.** American Journal of Psychiatry. 134(12):1371-1375, 1977.

The effects of a new antipsychotic agent, sulpiride, on serum prolactin and growth hormone levels were assessed among 16 chronically hospitalized, severely ill schizophrenic patients. Sulpiride is classed as an orthopramide or O-anisamide; its chemical name is N-((1-ethyl-2-pyrrolidinyl)-methyl)-2-methoxy-5-sulfamoylbenzamide. Findings indicate that this neuroleptic compound displayed definite evidence of antipsychotic activity while producing few adverse reactions. It is noted that the relative absence of extrapyramidal side-effects may indicate that unlike other neuroleptics, sulpiride has a low potential for producing tardive dyskinesia. Two patients who did not develop significant increases in prolactin levels did show a definite therapeutic response to sulpiride. Results lead to the conclusion that central dopaminergic blockade in the hypothalamic area is not a prerequisite for antipsychotic activity. 26 references. (Author abstract modified)

001555 Pearce, J. L.; Sharman, J. R.; Forster, R. M. Taranaki Base Hospital, New Plymouth, New Zealand **Phenobarbital in the acute management of febrile convulsions.** Pediatrics. 60(4, Part 2):569-572, 1977.

Blood levels of phenobarbital were determined after a single oral or intramuscular (IM) dose in children in the hospital after febrile convulsions. At a dose of 15mg/kg, both the oral and IM routes gave therapeutic blood levels within 90 minutes. Absorption from the IM route before 90 minutes was inconsistent and would be unlikely to arrest an established convulsion within a critical time period. For use as a drug to prevent convulsions, oral phenobarbital at 15mg/kg deserves further study. 13 references. (Author abstract)

001556 Tanaka, Masatoshi; Isozaki, Hiroshi; Inanaga, Kazutoyo. Kurume University, School of Medicine, Kurume 830, Japan **Effects of ID-540 on averaged photopalpebral reflex in man.** Japanese Journal of Pharmacology (Kyoto). 27(4):517-522, 1977.

Effects of ID-540, a recently introduced benzodiazepine derivative, on the averaged photopalpebral reflex (PPR), subjective symptoms and serum levels of ID-540 and its principal metabolite N-desmethyl-ID-540 following an oral does of 0.5mg were investigated in four healthy male Japanese students in their early twenties. Both the latencies of PPR, P1 and P2 latency, showed a prolongation and maximum level at 2 to 2.5hours after administration and tended to decline thereafter to control levels. The serum concentration of ID-540 showed a peak level at 2 hours after dosing, then showed a decline at 4 hours. The N-desmethyl-ID-540 exhibited a slow, gradual rise in the serum over the first 4 hours and there was a tendency toward a continued rise even at 24 hours. It is concluded that the PPR test may be a useful means of determining the clinical effects of anxiolytic agents and that ID-540 appears to be an agent with remarkable anxiolytic effects. 10 references. (Author abstract)

08 DRUG TRIALS IN SCHIZOPHRENIA

001557 Bjerkenstedt, Lars; Gullberg, Bo; Harnryd, Christer; Sedvall, Goran. Laboratory of Experimental Psychiatry, Dept. of Psychiatry, Karolinska Hospital, S-10401 Stockholm, Sweden **Relationships between clinical and biochemical effects of melperone and thiothixene in psychotic women.** Research Report, NIMH Grant MH-27254, 1977. 28 p.

Clinical and biochemical effects of melperone and thiothixene were studied in 49 psychotic women with schizophrenic symptomatology. Psychotic morbidity and side effects were determined by rating scales. Major monoamine metabolite concentrations were measured by mass fragmentography, and prolactin concentration was also determined before and after start of drug treatment. The drugs were similar in antipsychotic potency, but thiothixene treatment caused greater elevation of metabolites than melperone. Measures of dopaminergic activity did not correlate significantly with therapeutic outcome with either drug. In both treatment groups, clinical improvement correlated significantly with an increased 5-hydroxyindoleacetic acid/4-hydroxy-3methoxyphenylethylene glycol (MOPEG) ratio, and extrapyrimidal side effects correlated negatively with homovanillic acid (HVA) and HVA/MOPEG ratio in the thiothixene but not in the melperone group. It was concluded that there is no direct relationship between alteration of dopaminergic transmission and therapeutic outcome in drug treated psychotic patients. It is suggested that alteration of norepinephrine mechanisms may play a role in the antipsychotic effect. 35 references. (Journal abstract modified)

001558 Calil, Helena M.; Yesavage, Jerome A.; Hollister, Leo E. Dept. of Psychiatry, Stanford Univ. School of Medicine, Stanford, CA 94305 **Low dose levodopa in schizophrenia.** Communications in Psychopharmacology. 1(6):593-596, 1977.

Previous findings on the efficacy of levodopa in addition to conventional drugs for the treatment of schizophrenia (Inanaga, et al.,1975) led to an evaluation of low doses of levodopa (500mg) in three schizophrenics resistant to ongoing conventional treatment. Mental status and growth hormone were evaluated. There was worsening of symptoms in two of the three patients and one did not have a major clinical change. Data are discussed considering the dopaminergic hypotheses of schizophrenia. 12 references. (Author abstract modified)

001559 Chouinard, Guy; Annable, Lawrence; Cooper, Sam. Allan Memorial Inst., McGill University, Montreal, Canada **Antiparkinsonian drug administration and plasma levels of penfluridol, a new long-acting neuroleptic.** Communications in Psychopharmacology. 1(4):325-331, 1977.

The interaction of the antiparkinsonian drug (anticholinergic type) procyclidine HCl with a long-acting neuroleptic, penfluridol, was studied. Antiparkinsonian drugs have been shown to interact with neuroleptic drugs and reduce their effect. A 13 week study carried out in schizophrenic patients found a negative correlation between the blood levels of penfluridol, and the patients' dosage of procyclidine HCl (kemadrin). Procyclidine HCl did not, however, decrease the penfluridol plasma levels to an extent that interfered with the therapeutic effect of penfluridol. 12 references. (Author abstract modified)

001560 Davis, Glenn C.; Bunney, William E., Jr.; DeFraites, Emanuel G.; Kleinman, Joel E.; Van Kammen, Daniel P.; Post, Robert M.; Wyatt, Richard J. Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Intravenous naloxone administration in schizophrenia and affective illness.** Science. 197(4298):74-76, 1977.

To study the possible mood altering and antipsychotic effects of naloxone in patients with schizophrenia and affective illness fourteen schizophrenic patients and five patients with affective disorders were given naloxone or placebo intravenously in a double blind fashion. Physicians' ratings of hallucinations, mannerisms and posturing, conceptual disorganization, psychosis, and mood did not change significantly. A single item, unusual thought content, improved significantly on the naloxone day compared to the placebo day. There was no improvement in mood in affectively ill patients rated either by themselves or by physicians. Naloxone did not markedly improve any patient studied, which suggests that the acute blockade of opiate receptors is not associated with global improvement in psychotic symptomatology. 13 references. (Author abstract)

001561 Davis, J. M.; Garver, D. L.; Dekirmenjian, H.; Smith, R.; Casper, R. Illinois State Psychiatric Institute, Chicago, IL 60612 **The pharmacokinetics of red blood cell and plasma butaperazine clinical response and side effects.** Pharmacologist. 19(2):179, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, studies of the pharmacokinetics of red blood cell and plasma butaperazine levels and of the relationship between red cell levels of the drug and clinical response in schizophrenic patients were reported. In the first study, patients with schizophrenia were administered an initial single test dose of butaperazine followed by chronic twice daily administration. The pharmacokinetic parameters such as the area under the curve of plotted red cell and plasma butaperazine levels were highly predictive of steady state butaperazine levels. An inverted U-shape relationship was demonstrated between red cell levels and rate of clinical response as measured by changes on the New Haven Schizophrenia Index. In the second study, single dose peak height of newly admitted schizophrenics with fair to excellent clinical response were compared to those of a selected group of schizophrenics who showed neither side-effects nor therapeutic response to the drug. Peak heights were substantially higher in the clinically responsive patients than in the nonresponders. It is suggested that red cell levels are more closely related to psychiatric parameters, such as clinical response. (Author abstract modified)

001562 Davis, John M. Illinois State Psychiatric Institute, Chicago, IL **New antipsychotic drugs.** Current Psychiatric Therapies. 17:209-218, 1977.

The use of indoles and dibenzoxazepines for the treatment of schizophrenia is reviewed in regard to their relative efficacy. Data resulting from six controlled clinical studies of molindone (an indole) and from 13 studies of loxapine (a dibenzoxazepine) are presented in tabulated format. It is suggested that if a particular patient is resistant to the more commonly used antipsychotic phenothiazines, thioxanthenes, and butyrophenones, one of these two new drugs may have a slightly different metabolism or differ in some other property which would make it effective. 22 references.

001563 Fleischhauer, J. Psychiatrische Universitatsklinik, Wilhelm Kleinstrasse 25, CH-4025 Basel, Switzerland **Treatment of chronic schizophrenics with the oral long-term neuroleptic penfluridol in an open study.** Progress in Neuro-Psychopharmacology (Oxford). 1(1/2):135-140, 1977.

The effectiveness of the oral long-term neuroleptic penfluridol was investigated in 16 chronic schizophrenics under treatment for 8 weeks. Blood analysis, vegetative examinations, and ECG recordings were taken before and after the drug's administration. It showed a special influence on several factors that coregulate man's social accommodation, such as affectivity, affective report, and certain self-control functions, and had a positive influence on the symptoms of delusion. It proved to be an antipsychotic substance without sedative effects. Side-effects were generally rare and slight. It is suggested that penfluridol is suitable for the treatment of chronic schizophrenics during their rehabilitation. 6 references. (Author abstract modified)

001564 Hall, Peter. University of Birmingham, Birmingham, England **Choice of medical treatment in schizophrenia.** Practitioner (London). 219(1312):493-498, 1977.

The medical treatment of schizophrenia is discussed with reference to diagnosis, etiology and therapy. Schizophrenic symptoms defined by E. Bleeuler and Schneider are presented as criteria for distinguishing schizophrenia from other mental illness. Current treatment falls into a model that includes drug or other treatment of the acute illness, support of the ill patient himself, a period of convalescence or rehabilitation, and reassurance and help for relatives regarding the residual disabilities which often follow the illness. The various drugs which should be prescribed are discussed with reference to the various symptoms and suspected causes which each acts upon.

001565 Haring, C. Neuropsychiatrische Klinik Waldhaus Nikolassee, Am Waldhaus 1-19, D-1000 Berlin 38, Germany **/Long-term treatment of schizophrenia with penfluridol./ Langzeitbehandlung der Schizophrenie mit Penfluridol.** Medizinische Welt (Stuttgart). 28(13):639-642, 1977.

Side-effects of long-term treatment of schizophrenia with penfluridol were investigated. Penfluridol, a diphenylbutylpiperidine, is an oral neuroleptic of high potency with relatively low extrapyramidal motoric side-effects. Its potency persists for about a week, and sedative effects are not excessive. Empirical data were obtained from 62 female patients diagnosed as schizophrenic, paranoid in the involutional phase, and delusional. All patients were ambulatory and reported periodically for their penfluridol supply. The standard dosage was 20mg/week. After approximately 1 yr, 34 reported no side-effects, 19 had only initial akathisia, 9 reported slight restlessness, and 3 complained of severe symptoms. Other complications included initial fatigue (4), initial vision disturbances (3), tremor (2), loss of libido (2), reduced concentration (1), weight gain (7), general reduction in drive (5), and persistent tiredness (4). An indication of the acceptance which penfluridol has gained at the Waldhaus Nikolassee clinic in Berlin is the trend in prescriptions between 1971 and 1973: statistics show that in 1973 diphenylbutylpiperidines were prescribed for over half of released schizophrenics, and about 80% of this group received penfluridol. 21 references.

001566 Hymowitz, Paul. Adelphi University, Garden City, NY **Thought disorder in schizophrenia: a theoretical approach using an analysis of speech. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-25036 HC$15.00 MF$7.50 107 p.

To examine the effects of neuroleptic drugs on cognitive organization and self/object differentiation using a speech analysis approach, chronic schizophrenic inpatients were administered the Thematic Apperception Test, and object sorting task, and an adjective rating scale (the D-A-P Test) both with and without neuroleptic medication. Subjects tested in the off medication condition use shorter sentences, more frequent ungrammatical speech fragments, and score higher on a speech pathology scale. Speech analysis measures are sensitive to drug effects and to the cognitive and affective state of the speaker, have high interrater reliability, and correlate with other scales examining related mental phenomena. Further, results suggest that overinclusive thinking is not a major factor in the cognitive functioning of the chronic schizophrenic. Object/self differentiation is viewed as an important theoretical construct for understanding schizophrenic experience and function. Component factors of differentiation and the variable effects of medications in subjects varying in level of differentiation are also discussed. (Journal abstract modified)

001567 Matsuhara, Taro. Matsuhara Hospital, Matsuhara, Japan **Experiences with the continued use of psychotropic drugs.** Psychiatria et Neurologia Japonica (Tokyo). 79(3):165, 1977.

At the 73rd Northern Japan Symposium for Neuropsychiatrists held in January 1976 at the New Grand Hotel in Kanazawa, Japan, an experiment done, giving four injections of the anti-schizophrenic drug, furfenamine, to 104 schizophrenic patients who had not been effectively treated in the past with drugs and were not currently taking any medication. Average age of the patients was 35.8years, and they had schizophrenia for an average of 13.4years. Dosage was an average of 237.4mg. The drug was clearly effective in 3 (2.9%), slightly effective in 34 (32.7%), ineffective in 59 (56.7%), and caused a turn for the worse in 8 (7.7%). 37.75 experienced side-effects, and trembling fingers was the most prominent, followed by anxiety, hot flashes, thirst, decrease in white blood corpuscles, dyskinesia, and anemia.

001568 Simpson, Richard L. University of Kansas, Lawrence, KS **The effects of an antipsychotic medication on the classroom behavior of four schizophrenic male children.** Journal of Autism and Childhood Schizophrenia. 7(4):349-358, 1977.

An analysis of attention to task, deviant classroom behavior, and academic productivity data was conducted on four schizophrenic male children to whom an antipsychotic medication was administered. The psychiatrist in charge recommended that in each case the children be administered trifluoperazine (Stelazine). Although the results indicate varying degrees of success as a function of this psychotropic treatment, the medication appeared to have little influence on classroom behavior for three of the children. It is concluded that empirical strategies must be developed for objectively assessing the influence of medications administered for the purpose of controlling the classroom behavior of disturbed children. 9 references. (Author abstract modified)

001569 Smith, Robert C.; Dekirmenjian, H.; Davis, John M.; Crayton, J.; Evans, H. Manteno State Hospital, Manteno, IL **Plasma butaperazine levels in long-term chronic non-responding schizophrenics.** Communications in Psychopharmacology. 1(4):319-324, 1977.

Blood levels of butaperazine and other neuroleptics in schizophrenic patients who had consistently shown a lack of clinical response to antipsychotic drugs were compared to neuroleptic levels in newly admitted acute and relapsing schizophrenics who had a better response to treatment with antipsychotics. The chronic schizophrenic patients, who had been hospitalized for 3 to 20 years, had plasma levels of butaperazine after an acute 40mg dose which were significantly lower than the newly admitted schizophrenics. It is suggested that low blood levels of neuroleptics may be a factor in poor clinical response; studies are encouraged to determine whether the low blood levels are specific to butaperazine, or are a more general characteristic of chronic nonresponders. 8 references. (Author abstract modified)

001570 Tamminga, C. A.; Schaffer, M. H.; Crayton, J. W.; Davis, J. M. University of Chicago, Chicago, IL 60637 **Schizophrenic symptom remission with apomorphine.** Pharmacologist. 19(2):155, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a double-blind study of the acute effects of apomorphine in 18 patients with chronic schizophrenia was reported. Apomorphine reduced psychotic symptoms in these patients. It is suggested that apomorphine exerts its effects in schizophrenia by an action on presynaptic dopamine (DA) receptors resulting in decreased DA production. (Author abstract modified)

001571 Traficante, L. J.; Hine, B.; Gershon, S.; Sakalis, G. Dept. of Psychiatry, NYU School of Medicine, 550 1st Ave., New York, NY 10016 **Chloroquine potentiation of thioridazine effects in rats and drug-resistant schizophrenic patients: a preliminary report.** Communications in Psychopharmacology. 1(4):407-419, 1977.

Data on chloroquine potentiation of thioridazine effects in rats and drug resistant schizophrenics are presented. Chloroquine was found to potentiate the neuroleptic effects of thioridazine both in rats and schizophrenic patients, possibly by the inhibition of certain phenothiazine sulfoxidation metabolic processes. While chloroquine alone had very little pharmacological effect on rats, it significantly increased the

hypothermic, ptosis, and tail flick latency effects of this neuroleptic. Furthermore, when given after the onset of amphetamine induced stereotypy, it significantly increased the attenuating effect of thioridazine. Clinical trial of the chloroquine/thioridazine combination was tested on six schizophrenic patients who did not respond to thioridazine. Four of the patients characterized as nonparanoid schizophrenics rapidly improved with this treatment and were discharged in a few days; whereas the remaining two diagnosed paranoid schizophrenics who did not respond to this treatment improved when switched to perphenazine, and were later discharged. 30 references. (Author abstract modified)

001572 Yamauchi, Michi; Funatsu, Kunihiko; Nakamura, Jun; Nagata, Toshiyasu; Inanaga, Kazutoyo; Kai, Yasunobu. Department of Neuropsychiatry, Kurume University School of Medicine, Kurume 830, Japan **Effectiveness of Baclofen in schizophrenia.** Kurume Medical Journal (Kurume). 24(2):111-116, 1977.

The clinical course is observed in the administration of Baclofen in daily doses of 5mg to 45mg for 3 to 11 weeks to ten cases of schizophrenia whose duration of illness was 5.4years on the average. As to therapeutic effects, symptoms remained unchanged in nine cases and became aggravated in one case. Electroencephalographic examinations showed no tendency to improvement. The literature on the relationship between GABA and the DA metabolism and on the application of Baclofen to schizophrenia is discussed. 12 references. (Author abstract)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

001573 Adolphe, Allen B.; Dorsey, E. Richard; Napoliello, Michael J. Department of Pharmacology, Wright State University School of Medicine, Dayton, OH 45431 **The neuropharmacology of depression.** Diseases of the Nervous System. 38(10):841-846, 1977.

An illustrated review of the neuropharmacology of depression is presented, and eight chemical substances which have been characterized as neurochemical transmitters are listed together with the important steps in their synthesis and activation. The mechanisms of action of tricyclics, monoamine oxidase inhibitors, and psychostimulants on the adrenergic central receptors of the brain are summarized. The biochemical classification of depression is discussed also, noting that evidence is mounting for at least two biochemical subtypes of depression: 1) the norepinephrine depression, with low urinary MHPG levels, indicating a possible deficiency of norepinephrine in the CNS; and 2) the serotonin depression with normal or elevated MHPG levels and low cerebrospinal fluid 5-HIAA levels associated with a presumed CNS serotonin deficiency. 24 references.

001574 Amin, M. M.; Ban, T. A.; Lehmann, H. E. McGill University, Montreal, Quebec, Canada **Desipramine in the treatment of depression: a comparison of divided vs single dose administration.** Psychiatric Journal of the University of Ottawa (Ottawa). 2(3):117-119, 1977.

Comparison of divided versus single dose administration of desipramine in the treatment of depression carried out in a double-blind experiment with 20 psychiatric depressive outpatients is described. Results showed that clinically, single dose administration was as effective as a divided dose regimen. Findings also showed that a change from divided to single dose and vice versa did not result in any deterioration of the depressive psychopathology. No obvious difference was found in adverse effects in the two groups. A positive correlation was found between plasma levels and therapeutic efficacy. 5 references.

001575 Atanasio, G. Ospedale Psichiatrico S. Niccolo, Siena, Italy **/Intravenous combined administration of clorimipramine and sulpiride in depression./** L'uso, in associazione, della clorimipramina e della sulpiride, mediante perfusione venosa, nel trattamento delle depressioni. Rassegna di Studi Psichiatrici (Siena). 66(1):91-98, 1977.

A test of clorimipramine in association with sulpiride administered intravenously to a group of 30 depressive females, aged 23 to 68, for a 30 day to 40 day period, is described and evaluated. Patients exhibited various kinds of depression, including inhibition, guilt, anxiety, and apathy. Results show administration of the two drugs in combination is highly effective, with marked improvement noted after the first week of treatment. Very few side-effects were reported. 23 references.

001576 Biggs, John T.; Ziegler, Vincent E. Washington University School of Medicine, 4940 Audobon Ave., St. Louis, MO 63110 **Protriptyline plasma levels and antidepressant response.** Clinical Pharmacology and Therapeutics. 22(3):269-273, 1977.

The relationship between therapeutic response and protriptyline plasma levels in depressed patients attending an outpatient clinic was investigated. Twenty one depressed outpatients were treated for 4 wk with 20mg/day of protriptyline. Protriptyline plasma levels in individuals after 4 wk ranged from 22ng/ml to 167ng/ml. There was a negative correlation between the severity of depression measured by the Hamilton Rating Scale (HRS) and the wk 4 protriptyline concentration. Patients with plasma levels above 70ng/ml (wk 4) had better outcomes measured by the HRS and the Zung Self-Rating Depression Scale and had greater percent decreases on both scales during treatment than those with lower plasma levels. An upper limit to the therapeutic plasma level range beyond which response to treatment was less satisfactory was not demonstrated in this study. 21 references. (Journal abstract)

001577 Bowers, Malcolm B., Jr.; Heninger, George R. Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510 **Lithium: clinical effects and cerebrospinal fluid acid monoamine metabolites.** Communications in Psychopharmacology. 1(2):135-145, 1977.

The clinical effects of lithium treatment and its effects on cerebrospinal fluid (CSF) acid monoamine metabolites were measured in an experiment with manic-depressive, unipolar depressed, and schizoaffective patients. Lumbar CSF 5-hydroxyindoleacetic acid (5HIAA), homovanillic acid (HVA), and tryptophan were measured following the administration of probenecid in several groups of psychiatric patients before and during treatment with lithium. CSF 5HIAA was increased during lithium treatment but the increase was not correlated with lithium dose, serum lithium, duration of lithium treatment, or treatment response. Changes in CSF probenecid or tryptophan did not account for the increase in CSF 5HIAA. There was a significant positive correlation between pretreatment CSF 5HIAA and response to lithium. 18 references. (Author abstract modified)

001578 Brumback, Roger A.; Weinberg, Warren A. Department of Neurology, University of Pittsburgh School of Medicine, Pittsburgh, PA **Mania in childhood. II. Therapeutic trial of lithium carbonate and further description of manic-depressive illness in children.** American Journal of Diseases in Children. 131(10):1122-1126, 1977.

The therapeutic efficacy of lithium carbonate in six children diagnosed as manic who had responded poorly to treatment with tranquilizers was evaluated. Outpatient administration of lithium carbonate in dosages of 30 to 40mg/kg/day produced therapeutic blood lithium levels, and improved manic symptoms in all six children. Two of the children had a prolonged remission of symptoms with the lithium treatment. Lithium was discontinued in three patients whose depressive symptoms were uncontrollably worsened. Electroencephalographic epileptiform activity developed in one child receiving lithium carbonate. Using the strict diagnostic criteria for childhood mania, further therapeutic trials including double-blind studies are indicated to establish the proper role of lithium carbonate in the treatment of this disorder. A tabular listing of criteria for the diagnosis of mania and depression in children is also presented. 23 references. (Author abstract modified)

001579 Cooper, Allan J. Department of Psychiatry, St. Mary's Medical School, London, England **Tryptophan and affective disorders.** Scottish Medical Journal (Glasgow). 22(4):245-247, 1977.

The role of L-tryptophan, the amino acid precursor of 5-hydroxytryptamine (5-HT) is the pathogenesis and treatment of depression and other affective disorders is described by citing several case studies and experiments with psychiatric patients. In three separate studies, there was shown to be a significant positive correlation between plasma free tryptophan concentrations and mood state in depressives and postpartum women. In other studies, it was concluded that there was an association between mood and the concentration of tryptophan in the brain. In clinical psychiatry, the uses and limitations of tryptophan in the treatment of depression are becoming clearer. It is suggested that functional deficiency of 5-HT in certain parts of the brain underlie certain types of affective disorder, but that other neurotransmitters may also be concerned and that the ratio of one to the other may be critical. 16 references.

001580 Davidson, Jonathan R. T.; McLeod, Malcolm N.; Kurland, Albert A.; White, Helen L. Center for Interpersonal Studies, 3188 Atlanta Street, SE, Smyrna, GA 30080 **Antidepressant drug therapy in psychotic depression.** British Journal of Psychiatry (London). 131:493-496, 1977.

To examine the clinical efficacy of imipramine and phenelzine in the treatment of psychotic depression, 10 psychotic depressives (9 female, 1 male) were administered imipramine (90mg daily) or phenelzine (150mg daily) for 3 weeks. Imipramine and phenelzine were ineffective in the treatment of five primary unipolar depressives with delusions, even when plasma levels of imipramine and desmethylimipramine or activity of platelet monoamine oxidase suggested that an adequate dose of drug had been given. Four patients went on to receive ECT and all responded well. Five nondelusional patients responded satisfactorily to the antidepressant drug given. Nine out of ten subjects were women. Nondelusional patients showed some placebo response. ECT is considered to be the treatment of choice in the acute phase of delusional depression in women. 15 references. (Author abstract modified)

001581 De Bernardi, M.; Berte, F.; Lombardi, M.; Mazzella, G. L. Istituto di Farmacologia Medica dell'Universita di Pavia, Pavia, Italy **/Clinical and pharmacokinetic study of dibenzepine (Ecatril): comparison between the normal and retard forms./** Studio clinico e farmacocinetico della dibenzepina (Ecatril): confronto fra la preparazione normale e la nuova forma retard. Rassegna di Studi Psichiatrici (Siena). 66(1):99-110, 1977.

A clinical study was made of the antidepressant dibenzepine (Ecatril) in 24 male and female patients with endogenous, reactive, neurotic, and involutional depression, comparing ordinary and delayed action pills. Two groups of six males and six females 33 to 65 years of age were tested, and the period of treatment ranged from 10 to 35 days for the retard form and 10 to 40 days for the normal form of administration. Results show that the new retard form was more rapidly effective and better tolerated than the normal form, with the additional favorable feature that the retard form is administered only once per day. It is concluded that the retard form of dibenzepine (Ecatril) is preferred because of its convenience of administration. 13 references.

001582 Donnelly, Edward F.; Waldman, Ivan N. NIMH, William A. White Bldg., Saint Elizabeths Hospital, Washington, DC 20032 **IQ as a predictor of antidepressant responses to imipramine.** Psychological Reports. 41(1):54, 1977.

A study is reported which suggests that IQ score may be one of several predictors of response to the antidepressant drug imipramine. It is reported that patients who were assessed by clinical impression to be less intelligent than average may respond better to imipramine than patients above average intelligence. Computation of a critical value indicated that a full scale WAIS IQ of less than 106 was a responder to imipramine whereas 106 or greater was a nonresponder. Results need cross-validation. 3 references.

001583 Dunner, David L.; Patrick, Vijayalakshmy; Fieve, Ronald R. New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Rapid cycling manic depressive patients.** Comprehensive Psychiatry. 18(6):561-566, 1977.

Rapid cycling manic-depressive patients characterized by having four or more episodes of depression and/or mania per year prior to the initiation of lithium prophylactic treatment are described in clinical detail, and the effect of lithium prophylactic treatment on their clinical courses is illustrated. At the New York State Psychiatric Institute, rapid cycling patients were found to be indistinguishable from other bipolar patients on the basis of symptoms, age of onset, or family history and may likely represent one extreme of a continuum of episode frequency in bipolar illness. Data is cited to support the chronic use of lithium carbonate in rapid cyclers for, although the frequency of attacks may not be changed, the severity and duration of both the depressive and manic episodes seems to be ameliorated. An approach to the treatment of rapid cycling manic-depressive patients is described. 14 references.

001584 Edwards, J. Guy. Knowle Hospital, Fareham, Hants PO17 5NA, England **Viloxazine: assessment of potential rapid antidepressant action.** British Medical Journal (London). No. 6098:1327, 1977.

To assess the antidepressant effects of viloxazine, a placebo controlled trial was conducted using 29 moderately to severely depressed patients ranging in age from 18 to 61, who received either viloxazine or a placebo three times a day for 1 week. The Hamilton rating scale for depression, the Wakefield self-assessment depression scale and global assessments measured the drug's effectiveness. The results suggest that viloxazine is not as effective as a placebo. It is concluded that the results of previous trials, which suggest that viloxazine in a similar dosage has rapid antidepressant action, could be simply placebo responses. 5 references.

001585 Fabre, Louis F., Jr.; McLendon, David M.; Gainey, Allison. Fabre Clinic, 5503 Crawford St., Houston, TX **Double-blind placebo-controlled comparison of amoxapine and imipramine in depressed out-patients.** Current Therapeutic Research. 22(5, Sect. 1):611-619, 1977.

Ninety outpatients with a diagnosis of depression were entered in a 6 week trial using amoxapine, imipramine, or placebo. Both amoxapine and imipramine were effective in alleviating depression and superior to placebo after the second week of the trial. Both physician's and patient's rating scales showed similar results and the amoxapine group was indistinguishable from the imipramine group. Side-effects were similar for both groups but were less severe in the amoxapine group. 11 references. (Author abstract modified)

001586 Farber, Irving J. Booth Memorial Medical Center, Flushing, NY 11355 **Manic-depressive psychoses.** New York State Journal of Medicine. 77(12):1904-1905, 1977.

The incidence of diagnosis of manic-depressive psychosis is traced across the years since 1920, and related to the increased use of lithium in the treatment of the disorder. In past years there has been a steady decline in the incidence of manic depressive psychoses. More recently, with the use of lithium in treating this illness, and the marked increase in the medical and nonmedical literature concerning manic depressive psychoses, the impression has been that the incidence is much higher than in the past. However, careful study of the illness shows that there has not been any significant rise in the incidence of manic-depressive psychoses. 13 references. (Author abstract modified)

001587 Furlong, F. W.; Sellers, E. M.; Kapur, B. M. Department of Psychiatry, Toronto Western Hospital, Toronto, Ontario, Canada **Amitriptyline blood levels and relapse.** Canadian Psychiatric Association Journal (Ottawa). 22(6):275-284, 1977.

Blood levels of the tricyclic antidepressants amitriptyline and nortriptyline resulting from oral dosage were studied and the patient relapse rate over a six month period was analyzed. Nine previously depressed patients who had responded either to amitriptyline, nortriptyline, or ECT, were followed for six months on two different dosages of amitriptyline daily, double-blind. The range of blood concentration was as expected and no specific relationship was found between variations in blood levels and depression scores from one assessment to the next for the nine patients. Two patients relapsed within six months. Of the two, one showed the highest blood levels and the other showed very low blood levels. It is concluded that these results support the view that lack of effectiveness of these drugs may be associated with too high or too low blood levels; that relapse may also be associated with very high or very low blood levels; and that the use of even rough measuring of blood levels could indicate which alternative was more likely in a given individual. 27 references. (Author abstract modified)

001588 Ghose, K.; Coppen, A. MRC Neuropsychiatry Lab, West Park Hospital, Epsom, Surrey, England **Noradrenaline, depressive illness, and the action of amitriptyline.** Psychopharmacology (Berlin). 54(1):57-60, 1977.

The relationship between the reuptake blocking effect of noradrenaline by amitriptyline, and its therapeutic effect on depressed patients were investigated using the tyramine dose/pressor response test on 23 patients suffering from primary depressive illness before and during treatment with amitriptyline. The decreased tyramine sensitivity induced by the drug, which is related to the inhibition of noradrenaline reuptake, correlated significantly with the plasma concentration of nortriptyline. However, contrary to the expectation of the noradrenaline hypothesis of depression, the decreased tyramine sensitivity did not show any correlation with clinical improvement following 6 weeks' treatment with amitriptyline. Evidence from the present and previous studies which bring the noradrenaline hypothesis of depression is discussed. 25 references. (Author abstract modified)

001589 Goldberg, Harold L.; Finnerty, Richard J. West-Ros-Park Mental Health Center, Boston, MA **Which tricyclic for depressed outpatients, imipramine pamoate or amitriptyline?** Diseases of the Nervous System. 38(10):785-789, 1977.

Imipramine pamoate and amitriptyline were compared in 57 neurotically depressed outpatients with sleep disturbance who were randomly assigned to treatment with either drug in a single dose at bedtime in a double-blind study for 4 weeks. The results indicate that both imipramine pamoate and amitriptyline are equally effective in treating neurotic depression. The clinical lore that imipramine is more effective for retarded depression and amitriptyline for anxious, agitated depression was not supported. The imipramine pamoate group had significantly earlier rising times, and a trend toward better quality of sleep. The side-effect profiles of the two drugs were also remarkably similar in this population though more patients complained of side-effects on amitriptyline than on imipramine. 19 references. (Author abstract modified)

001590 Gregoire, F.; Brauman, H.; de Buck, R.; Corvilain, J. Institut de Psychiatrie, Hopital Universitaire Brugmann (U.L.B.), 4, place Van Gehuchten, 1020 Brussels, Belgium **Hormone release in depressed patients before and after recovery.** Psychoneuroendocrinology (Oxford). 2(3):303-312, 1977.

In 19 deeply depressed patients suffering from primary affective disorders, the thyroid stimulating hormone (TSH) and prolactin (hPRL) responses to thyrotrophin releasing hormone (TRH) were measured. In ten of them, the growth hormone (hGH) and cortisol responses to hypoglycaemia (ITT) were also determined. In the depressed state, TSH secretion was extremely low or nonexistent and hPRL was below normal. Half of the tested patients had zero or subnormal hGH secretion in response to hypoglycaemia. After recovery, 16 of these patients were retested by TRH injection. TSH responses showed a fourfold increase and hPRL showed an increase of 45%. In the seven retested by ITT, the hGH response was not different, but the three previous nonresponders, herein included, were normalized. In all seven, the fall in glycaemia was more marked and the cortisol discharge was more sustained. These findings draw attention to: a) the high frequency of alterations in the functional endocrine tests in depressed patients, b) the discrepancy between these observations and the absence of any overt clinical signs of endocrine disease in these subjects, c) the interest in using the patient as his own control, and d) the reversible nature of these alterations after recovery. 35 references. (Author abstract)

001591 Herzberg, Louis; Herzberg, Brenda. Department of Medicine, University of Western Australia, Nedlands, W.A., Australia **Mood change and magnesium: a possible interaction between magnesium and lithium?** Journal of Nervous and Mental Disease. 165(6):423-426, 1977.

A significant sex difference in mean plasma magnesium levels found in an investigation of 20 male and 24 female depressive patients is reported, and the possible relationship

between magnesium and lithium is discussed. The difference in mean plasma magnesium levels was not found in controls or in calcium levels in the same patients. The difference could not be explained by previous treatment, type of symptoms or duration of illness. Further studies of magnesium metabolism are recommended to provide a better understanding of manic-depressive disease and the mode of action of lithium. 16 references.

001592 Kishimoto, Akira; Nakazawa, Kazuki; Kunimoto, Norifumi. Department of Neuropsychiatry, Tottori University, Tokyo, Japan **Flicker values and changes in states of depression.** Psychiatria et Neurologia Japonica (Tokyo). 79(4):211, 1977.

In a paper read at the 26th Central Japan Shikoku Symposium of Neuropsychiatrists, November 1976, Okayama, Japan, flicker values, were measured in 22 depressed patients and compared with those of 16 normal individuals. It was found that as the state of the depression patients improved, the flicker values rose. Moreover, the rise was parallel to that of the patients' clinical improvement. This was thought to be influenced by treatment with tricyclic antidepressants. After injection of imipramine in 10 depressed patients, flicker values in 8 Ss increased 102% over the noninjected control group. Imipramine had no such effect on the normal group, and their values lowered to 98% of the preinjection level.

001593 Knauth, Percy. no address **Depression -- the silent scream.** Rotarian. 131(4):26-29, 1977.

An overview is presented of the magnitude of depression as a public health problem, focusing on treatment innovations such as the community mental health center and the development of antidepressant drugs. It is concluded that the community mental health center embodies the new world of treatment available for the mentally ill and is a negation of the old world concept of long-term confinement in institutions.

001594 Kupfer, David J.; Hanin, Israel; Spiker, Duane G.; Grau, Thomas; Coble, Patricia. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Amitriptyline plasma levels and clinical response in primary depression.** Clinical Pharmacology and Therapeutics. 22(6):904-911, 1977.

In a study of amitriptyline plasma levels and clinical response in primary depression, 16 patients with primary depression were treated for 4 weeks with amitriptyline. After clinical diagnoses were determined, patients entered a double-blind protocol (amitriptyline or placebo) and their clinical status was determined with the Hamilton Depression Rating Scale by raters blind to the drug type, its dosage, and plasma levels. Amitriptyline and nortriptyline plasma levels were assayed twice weekly by gas chromatography/mass spectrometry. In the 16 patients a negative correlation between the Hamilton Score and the mean total tricyclic level as well as with individual plasma levels, was found at the end of the treatment period. When the group was divided into clinical responders and nonresponders, the mean total tricyclic levels discriminated the two groups by day 12 as well as at the end of the protocol. These results strongly suggest the presence of a positive correlation between plasma levels and clinical improvement in patients with primary depression. 16 references. (Author abstract modified)

001595 Kurland, Albert A.; Arana, Jose D. Maryland Psychiatric Research Center, Baltimore, MD **Drugs and depression: dosage and blood level monitoring.** Current Psychiatric Therapies. 17:179-188, 1977.

An overview of quantification methodology and correlates of interpretation of data of the pharmacological effects of drugs used in the treatment of depressions and various pharmacokinetic studies is presented. Studies of plasma levels of antidepressant medications as a means for relating the therapeutic activity of the drug to its plasma concentration are reported, and important areas for needed research investigations as yet not conducted are listed. Priority studies in clinical drug usage measurement are seen to be: 1) the steady state plasma levels and the relationship to the clinical efficacy of treatment; 2) the effect of the administration of other drugs and substances on the plasma level; and 3) the relation of the plasma level to the incidence and severity of side-effects. It is suggested that the results of these studies will provide criteria as to the adequacy of dosage and justification for medication alteration. 42 references.

001596 Leichter, Steven B.; Kirstein, Larry; Martin, Neil D. Dept. of Medicine, University of Kentucky College of Medicine, Lexington, KY 40506 **Thyroid function and growth hormone secretion in amitriptyline-treated depression.** American Journal of Psychiatry. 134(11):1270-1272, 1977.

Changes in indices of thyroid functioning were studied in 11 female patients and the effectiveness of L-dopa as a stimulus of growth hormone secretion was studied in another group of depressed subjects, before and after the inception of amitriptyline therapy. The stimulation of growth hormone secretion was unaffected by the amitriptyline therapy. The drug also caused no significant alteration on indices of thyroid functioning; however, scores on the Hamilton Depression Rating Scale were shown to improve significantly after the inception of therapy. It is suggested that thyroid function tests in patients taking amitriptyline are reliable indices of thyroid function in these patients and that L-dopa can be used to evaluate growth hormone secretion in these patients as well. 12 references.

001597 Nielsen, J. Lanng; Pedersen, E. B.; Amdisen, A.; Darling, S. Psychiatric Research Unit, Psychiatric Hospital, DK-8240 Risskov, Denmark **Reduced renal calcium excretion during lithium therapy.** Psychopharmacology (Berlin). 54(1):101-103, 1977.

In a study of the effect of lithium therapy on renal calcium excretion in ten depressive subjects, renal excretion of calcium was determined before and at intervals during 3 months of lithium treatment. The calcium excretion fell by more than 40% within the first week of treatment and remained low throughout the treatment period. The reduction in urinary calcium excretion could be accounted for by an increase in fractional tubular reabsorption of calcium. There were no changes in serum calcium or inorganic phosphate, nor in urinary inorganic phosphate. The results indicate that lithium interferes with the regulation of calcium metabolism. 10 references. (Author abstract modified)

001598 Panter, Barry M. Suite 600, 2701 West Alameda St., Burbank, CA 91505 **Lithium in the treatment of a child abuser.** American Journal of Psychiatry. 134(12):1436-1437, 1977.

The use of lithium in the treatment of a woman who abused her children is reported. The woman presented had changes of mood consistent with cyclothymic personality or manic-depressive illness. Lithium decreased the intensity of her emotions and allowed her to control her behavior, and therefore, develop her ego. As she gained an understanding of herself and her relationships, her anxiety diminished and she related to others with less distortion of reality and less aggression. 4 references.

001599 Pedersen, E. B.; Darling, S.; Kierkegaard-Hansen, A.; Amdisen, A. Dept. of Medicine C, Aarhus Kommunehospital, DK-8000 Aarhus C, Denmark **Plasma aldosterone during lithium treatment.** Neuropsychobiology (Basel). 3(2-3):153-159, 1977.

Plasma aldosterone, and serum and urine electrolytes were determined in nine manic-depressive patients before and at several intervals during 3 months of lithium treatment. The same determinations were carried out in 27 manic-depressive patients who had been treated with lithium for 3 months to 20 years and also in a control group. There was no change in plasma aldosterone during the longitudinal study and no difference between patients and controls in the transversal study. The latter study revealed, however, a positive correlation between serum lithium and plasma aldosterone. It is concluded that nontoxic lithium doses may produce slight sodium depletion in patients, which may in turn lead to a compensatory increase in aldosterone secretion and rising plasma aldosterone levels. 9 references. (Author abstract modified)

001600 Prien, Robert F.; Caffey, Eugene M., Jr. NIMH, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857 **Long-term maintenance drug therapy in recurrent affective illness: current status and issues.** Diseases of the Nervous System. 38(12):981-987, 991-992, 1977.

Current status and issues in long-term drug therapy in recurrent affective illness are assessed, noting that six comparative studies of lithium carbonate and short-term studies of tricyclic antidepressants in long-term maintenance drug therapy for affective illness document the effectiveness of lithium preventing or attenuating manic recurrences in bipolar affective illness. Studies also suggest that imipramine is just as effective as lithium in bipolar affective illness. Little information exists as regards the long-range effectiveness of drugs other than lithium or imipramine, and there are no dose reponse studies to guide the practitioner in adjusting dosage, nor is there sufficient information on the effectiveness of long-term maintenance chemotherapy in unipolar recurrent affective illness. Thus, although there has been a large quantity of research on long-term drug therapy in recurrent affective illness, critical questions still remain unanswered, and further evaluation must be made. 83 references.

001601 Priest, R. G. St. Mary's Hospital Medical School, London, England **Choice of antidepressants.** Practitioner (London). 219(1312):487-490, 1977.

A review of the factors involved in the selection of antidepressants is presented with reference to the various drug groups available and the uses and side-effects of each. The first choice is usually taken from among the tricyclic antidepressants, relatively safe drugs for which addiction does not occur. The use of monoamine oxidase inhibitors, L-tryptophan, flupenthixol, and lithium is briefly reviewed, noting side-effects and the danger of cross-prescription. Antidepressant prescription is considered a delicate matter for which there are no rules and for which the prescribing practitioner must use his skill and his discretion. 6 references.

001602 Saletu, B.; Strobl, G.; Grunberger, J.; Szeless, S.; Ferner, U. Section of Pharmacopsychiatry, Psychiatrische Universitatsklinik Wien, Lazaretsgasse 14, A-1090, Wien, Austria **Intensive antidepressive therapy by 48 hour slow-drip infusion with high doses dibenzepine.** Progress in Neuro-Psychopharmacology (Oxford). 1(1/2):125-133, 1977.

The onset of response, the degree of effectiveness, and side-effects of a 48 hour slow drip infusion of high doses of dibenzepine during intensive antidepressive therapy was investigated in 12 severely endomorphous depressed patients. Initial treatment with slow drip infusion was followed by 3 weeks of oral dibenzepine on an individual basis. This treatment procedure proved to be safe and highly effective with a rapid onset of action. The patients showed statistically significant improvement in depressive symptomatology as rated by the Hamilton Score as early as 24 hours after the start of treatment. Maximal improvement occurred around the sixth day of therapy, which was also substantiated objectively and quantitatively by psychological tests. The psychological tests indicated a marked improvement in attention, concentration, and psychomotor activity at the end of the infusion period. Evaluation of side-effects, ECG, blood pressure, heartrate, and laboratory findings indicate that there were few negative side-effects. 13 references. (Author abstract modified)

001603 Schneider, Melinda A.; Brotherton, Patricia L.; Hailes, Jean. Dept. of Psychology, University of Melbourne, Melbourne, Australia **Effect of exogenous oestrogens on depression in menopausal women.** Medical Journal of Australia (Glebe). 2(5):162-163, 1977.

A study of the effects of conjugated estrogens (Premarin) upon the depression scores of depressed and nondepressed menopausal women was carried out. Depression levels were obtained for both groups before and after four weeks of hormone replacement therapy. The Beck Depression Inventory (BDI) was used to assess depression levels, while a semistructured interview provided information related to the physiological, psychological and sociocultural stresses affecting individual women. Depression scores of the depressed group did not improve within the given treatment period, in contrast with improved scores for the nondepressed subjects who reported increased feelings of well-being following hormone replacement therapy. 9 references. (Author abstract)

001604 Sharma, S. D.; Nandkumar, V. K. Department of Psychiatry, Goa Medical College, Panaji, Goa, India **A comparison of a divided and a single dose regime of dothiepin and its therapeutic effectiveness.** Indian Journal of Psychiatry (Poona). 19(2):92-96, 1977.

A comparison of divided and single dose regimes of dothiepin and their therapeutic effectiveness was conducted in 20 adult patients suffering from depression. The patients were randomly allocated either to thrice daily doses or a single nocturnal dose over 4 weeks, with at least 2 weeks spent as an inpatient. No significant differences were seen between the thrice daily and the single nocturnal dosage regimes. The findings suggest that the response to dothiepin was good and the drug was well tolerated. 12 references.

001605 Shaw, David M. Department of Psychological Medicine, Welsh National School of Medicine, Whitchurch Hospital, Cardiff CF4 7XB, Wales **The practical management of affective disorders.** British Journal of Psychiatry (London). 130:432-451, 1977.

The psychopharmacological treatment of episodes of affective disorder commonly referred to the psychiatrist is discussed. Antidepressants, hypnotics, tranquilizers and electroconvulsive therapy (ECT) are among the treatment modalities discussed. The pharmacological aspects of tricyclic antidepressants, monoamine oxidase inhibitors (MAOI) and tryptophan are examined. The use of tranquilizers and ECT is reviewed and new antidepressants such as flupenthixol,

maprotiline, mianserin, viloxazine, trazodone and nomifensine are briefly mentioned. It is noted that the present state of research in affective disorder heralds the development of new techniques in treatment. 76 references.

001606 Standal, J. E. Department of Psychiatry, Fylkessjukehuset, Alesund, Norway **Pizotifen as an antidepressant.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(4):276-279, 1977.

The therapeutic effect and tolerance of pizotifen was compared in a double-blind study with placebo in 20 outpatients of both sexes suggering from light to moderate depression. Pizotifen seems to possess certain antidepressive effects in dosages of 4 to 10mg daily. These properties, and the well documented effect of pizotifen in migraine, could make it an alternative in treating patients suffering from the often seen combination of vascular headache/depression. 4 references. (Author abstract)

001607 Sullivan, John L.; Cavenar, Jesse O., Jr.; Maltbie, Allan; Stanfield, Charles. Psychiatry Service, Veterans Administration Hospital, 508 Fulton St., Durham, NC 27705 **Platelet-monoamine-oxidase activity predicts response to lithium in manic-depressive illness.** Lancet (London). No.8052/3:1325-1327, 1977.

The relationship between platelet monamine oxidase activity and response to lithium treatment was investigated among 24 manic-depressive patients. After the initial behavioral ratings and enzyme activity determination, each patient was given lithium and a standard dose of a neuroleptic agent. The neuroleptic was discontinued after the first week and the lithium treatment continued for 3 weeks. The results suggest that platelet monoamine oxidase activity predicts lithium response in manic-depressive illness. Mean enzyme activity was essentially the same in the treatment responsive subgroup as in the controls, whereas the treatment refractory subgroup had a mean enzyme activity significantly lower than both the controls and the treatment responsive subgroup. 9 references.

001608 Welner, Amos; Welner, Zila; Leonard, Mary Ann. Washington University School of Medicine, 4940 Audubon Avenue, St. Louis, MO 63110 **Bipolar manic-depressive disorder: a reassessment of course and outcome.** Comprehensive Psychiatry. 18(4):327-332, 1977.

Research literature on the course and outcome of patients with bipolar manic-depressive illness is reviewed, to ascertain whether the general positive consensus toward the successful treatment of this kind of mental illness is accurate. The total number of patients in these studies was 550 and length of followup ranged from 6 months to 25 years. It is concluded that the consensus that these patients have a favorable course and outcome was overly optimistic. Whether the determinants of morbidity were the presence of symptoms, social decline or both, a substantial minority of patients appeared to be chronically sick. In addition, some of the patients who did not have a chronic course suffered a permanent decline in their social and occupational status as a result of repeated episodes and hospitalizations. It is realized that treatment of patients with bipolar affective disorder with lithium salts may potentially modify the course of illness issue of chronicity irrelevant; but it is argued that the extent to which lithium is a real breakthrough in treatment of bipolar illness at the present time is still unsettled. 32 references. (Author abstract modified)

001609 Wilson, Ian C.; Loosen, Peter T.; Pettus, Charles W.; Lara, Patricio P.; Prange, Arthur J., Jr.; Wilson, Graham C. North Carolina Division of Mental Health Services, Raleigh, NC **A double-blind clinical comparison of amoxapine, imipramine, and placebo in the treatment of depression.** Current Therapeutic Research. 22(5, Sect. 1):620-627, 1977.

Twenty two inpatients suffering from severe primary depression were randomly assigned to three treatment modalities: amoxapine, imipramine, placebo. No significant differences occurred between treatment groups as regards selective criteria. Previous studies have doubted the effectiveness of amoxapine's anxiolytic properties and have also questioned the rapidity of onset of therapeutic activity. It is concluded that this study shows statistically that amoxapine possesses efficacious anxiolytic properties and its therapeutic activity is more rapid in onset than the other treatment modalities. 10 references. (Author abstract)

001610 Wirz-Justice, Anna. Psychiatrische Universitatslinik Basel, Wilhelm-Klein-Strasse 27, CH-4025 Basel, Switzerland **Theoretical and therapeutic potential of indoleamine precursors in affective disorders.** Neuropsychobiology (Basel). 3(4):199-233, 1977.

Research studies investigating the strategy of loading with precursor amino acids of the monoamines, postulated to be involved in the affective disorders, are reviewed. Phenylalanine, tyrosine, L-dopa, L-tryptophan and L-5-hydroxytryptophan (L-5-HTP) were found to induce differential behavioral and biochemical effects in both healthy subjects and endogenous depressives. Indoleamine precursors predominantly caused mood changes. However, it is argued that the efficiency of these amino acids as antidepressants was neither clearly established nor refuted due to insufficient consideration of the following criteria: 1) sufficiently high plasma levels to be taken up into the brain; 2) effective stimulation of serotonergic systems; and 3) selective increase of serotonin turnover with minimal interaction with other neurotransmitters. It is suggested that the use of intravenous L-5-HTP as a provocative test in depressive patients with concomitant neuroendocrinological and psychometric measurements, may be a method of adequately fulfilling these requirements. 109 references. (Author abstract modified)

001611 Yorkston, N. J.; Gruzelier, J. H.; Zaki, S. A.; Hollander, D.; Pitcher, D. R.; Sergeant, H. G. S. Friern Hospital, New Southgate, London N11 3BP, England **Propranolol in chronic schizophrenia.** Lancet (London). No. 8047:1082-1083, 1977.

Results are reported of an open study of 55 chronic schizophrenic patients given propranolol, in which chronicity did not seem to alter the proportion in whom schizophrenic symptoms remitted after more than 5 years. A control group of five patients given placebo was used to determine if the improvement came from reducing unwanted extrapyramidal effects of the major tranquilizers, rather than reducing the symptoms of schizophrenia; and if the same results would be achieved by reducing the dose of the major tranquilizers. Contrary to expectations, it was found that the two groups did not differ significantly in systolic or diastolic blood pressure and that the pulse rate did not consistently distinguish the propranolol group. It is suggested that more studies are needed to define the place of propranolol in the treatment of schizophrenia.

10 DRUG TRIALS IN NEUROSES

001612 Csillag, E. R. Department of Psychiatry and Behavioural Science, University of Western Australia, Nedlands, W. A. 6009, Australia /**Clinical report of the drug**

Tranxene (clorazepate dipotassium)./ Tranxene. Medical Journal of Australia (Glebe). 2(6):196, 1977.

A report of the successful treatment of 55 patients for recurring chronic anxiety state and/or somatic manifestations of anxiety with a single night dosage of Tranxene (clorazepate depotassium), is presented. The clinical impression gained during the one year period reported, is that tranxene is an excellent anxiety reducing drug. The importance of the once nightly dosage for improved drug taking behavior is emphasized. The most important factor in improving previous drug taking behaviors was the ease with which these patients managed to achieve sleep and therefore did not require an extra dose of medication before going to sleep. 2 references.

001613 Moore, Daniel C. Department of Psychiatry, Yale University School of Medicine, 34 Park Street, New Haven, CT 06508 **Amitriptyline therapy in anorexia nervosa.** American Journal of Psychiatry. 134(11):1303-1304, 1977.

The effect of amitriptyline in a patient with anorexia nervosa is described. A 20-year-old female presented complaining of multiple daily eating and vomiting episodes. She displayed a preoccupation with thinness even after her weight had decreased from 63.6kg (160cm height) to 47.7kg. After unsuccessful use of diphenylhydantoin and imipramine in conjunction with psychotherapy, amitriptyline therapy was started. Her vomiting behavior decreased markedly, and her weight increased to 52.2kg, normal for her height. After discontinuation of the drug, bulimia and vomiting recurred, and the medication was reinstated to obtain relief. The success with amitriptyline in this case, where imipramine therapy had failed, suggests that drugs which prevent reuptake of 5-hydroxytryptamine (5-HT) and decrease its turnover in the brain may be useful in treating anorexia nervosa. Weight gain and normalization of mood were also reported in six previous cases of anorexia nervosa with amitriptyline therapy. 10 references.

001614 Poole, A. Desmond; Csillag, E. R. Dept. of Psychiatry & Behavioral Science, Perth Medical Centre, University of Western Australia, Nedlands, Western Australia 6009, Australia **Declining diazepam desensitization therapy.** Journal of Behavior Therapy and Experimental Psychiatry. 8(3):301-303, 1977.

The use of high and gradually diminishing doses of diazepam (Valium) in the desensitization of a severe travel phobia is described. The patient was a 41-year-old woman who was referred for behavioral therapy because of a severe travel phobia, stemming from a minor accident. A treatment procedure was developed in which she was administered a dose of Valium and 2 hours later attempted to describe various images related to travel. Six hours after the first dose she received a second, stronger dose, and again, 2 hours later, she described travel related scenes. The program was continued for 5 days with actual driving sessions being added. The treatment was entirely successful and followup 6 months later indicated that the change was durable. 12 references.

001615 Takeyama, Eiji; Amano, Keishi; Kitamura, Koichi. Neurosurgery, Neurology Center, Tokyo Woman's School of Medicine, Tokyo, Japan **Experiences with using the anti-depressant dibenzepin:Noveril, on neurology outpatients.** Journal of the Japan Medical Association (Tokyo). 78(1):62-65, 1977.

The antidepressant dibenzepin (Noveril) was tested on 20 neurosurgery outpatients to determine effects on symptoms of muscle contraction, or pain from external head injuries. Patients were selected on the basis of neurological observations, head X-rays, brain waves, and computed tomography. Main symptoms included insomnia, droopy eyes, appetite loss, lowering of sexual desire, and fatigue. Dosage was three 80mg capsules/day and was continued for at least 14 days. All 20 patients had psychological depression. The drug was found effective in physical and psychological symptoms in 85% of the cases. It was seen as a safe drug if treatment was also given for the side-effect of low blood pressure. 3 references.

001616 Yaryura-Tobias, Jose A.; Bhagavan, Hemmige N. North Nassau Mental Health Center, 1691 Northern Blvd., Manhasset, NY 11030 **L-tryptophan in obsessive-compulsive disorders.** American Journal of Psychiatry. 134(11):1298-1299, 1977.

The therapeutic effectiveness of L-tryptophan in controlling obsessive-compulsive symptoms is examined. Seven obsessive-compulsive patients ranging in age from 13 to 40 were placed on L-tryptophan, 3 to 9g/daily in divided oral doses. Patients also received oral daily divided doses of nicotinic acid and pyridoxine. The patients showed considerable improvement in symptoms after 1 month of therapy, and were stabilized after 6 months to 1 year of therapy. The rationale for the use of L-tryptophan was based on successful experimentation with chlorimipramine in obsessive-compulsive disorders. It is believed that the effect of chlorimipramine, as a potent serotonin (5-HT) reuptake blocker, is mediated by a serotonergic mechanism. By using L-tryptophan, a precursor of 5-HT, an increase in steady state levels of serotonin in specific areas of the brain was accomplished. The nicotinic acid and pyridoxine were given to ensure that a maximum of tryptophan was available for 5-HT synthesis by inhibiting metabolic pathways of tryptophan. The data support the hypothesis that some obsessive-compulsive disorders are organic in nature and may be related to a central disturbance in 5-HT metabolism. An increase in aggressive behavior in two cases in which there was a history of aggressiveness contraindicates tryptophan treatment in such cases. 7 references.

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

001617 Davies, Gaius; Hamilton, Susan; Hendrickson, Elaine; Levy, Raymond; Post, Felix. Dept. of Psychological Medicine, King's College Hospital, Denmark Hill, London SE5 9RS, England **The effect of cyclandelate in depressed and demented patients: a controlled study in psychogeriatric patients.** Age and Ageing (London). 6(3):156-162, 1977.

In a double-blind clinical trial the effects of the vasodilator drug cyclandelate (in a dose of 1200mg daily) were studied in a group of 102 psychogeriatric patients with depressive illnesses or dementing conditions. The measures used before treatment and after 6 weeks' treatment were: clinical ratings, psychometric tests, cortical evoked potentials, the sedation threshold and the Gresham Questionnaire. In the depressive group there was no significant difference in the changes in scores at 6 weeks in three groups: those who received cyclandelate plus amitriptyline, those who received placebo plus amitriptyline, and those who received neither placebo nor cyclandelate. In the demented group there were significant changes in favor of the placebo on two measures, the Digit Copying test, and one component of the auditory evoked response. The results do not support the previously reported views claiming, in a number of studies, a significant improvement in the performance of both demented and normal elderly subjects treated with cyclandelate. The significance of these findings is discussed. 18 references. (Author abstract modified)

001618 Doongaji, D. R. Seth G. S. Medical College and K. E. M. Hospital, Parel, Bombay 400 012, India **The treatment of tardive dyskinesia with penfluridol.** Neurology India (Bombay). 25(4):244-246, 1977.

The successful treatment of a case of tardive dyskinesia with penfluridol following prolonged phenothiazine therapy is described. A 28-year-old male presented with symptoms diagnosed as acute schizophrenia, and therapy with chlorpromazine was initiated and later supplemented with trifluoperazine and trihexyphenydyl. After 36 months of phenothiazine treatment, the patient manifested repetitive, stereotyped grimacing movements diagnosed as tardive dyskinesia. Penfluridol therapy decreased both psychotic symptoms and dyskinetic movement. Results are discussed in terms of the probable effect of penfluridol on dopaminergic synapses. 10 references.

001619 Drury, K.A.D.; Spalding, E.; Donaldson, D.; Rutherford, D. Dept. of Obstetrics, Redhill General Hospital, Redhill, Surrey, England **Floppy-infant syndrome: is oxazepam the answer?** Lancet (London). No.8048:1126-1127, 1977.

In a letter to the editor, the use of oxazepam instead of diazepam in preeclampsia to offset development of floppy infant syndrome is explored. Because oxazepam has a short half-life and no known biologically active metabolites, it might be expected to be a safer drug than the parent drug, diazepam, in the management of preeclampsia. Oxazepam crosses the placenta and at time of delivery concentrations are usually higher in cord blood than maternal blood. No case of floppy infant syndrome has been encountered in 30 pregnancies managed by daily divided doses of oxazepam. It is concluded that a dose of up to 75mg a day is safe and particularly useful in pregnant women with moderate preeclampsia to tide the patient over to near maturity. 8 references.

001620 Gaspard, F.; Levy, A. no address **/Application of statistics to the methodology of studies of drugs acting on the brain./** Application de la statistique a la methodologie des etudes de medications a visee cerebrale. Revue de Geriatrie (Paris). 2(2):227-231, 1977.

A study of the effects of pyridinol carbamate on geriatric patients, average age 80, without pronounced deteriorative symptoms, revealed no clinical difference between drug group and control group until factor analysis of psychometric tests was applied. In a hospice environment 60 patients were observed for 6 months, and 50 of them were observed for 12 months. They were randomly divided into two groups, one receiving 1g/day pyridinol carbamate, and the other placebo. Greatest effects were noted in memory and attention tests, as well as in independence and interest in others. Results reveal that pyridinol carbamate exhibited preventive action, retarding the development of atherosclerotic lesions, and it is suggested pyridinol carbamate treatment begin before advanced age in geriatric patients. 12 references.

001621 Glatt, M. M. UCH Alcoholism Outpatient Centre, St. Paneras Hospital, London NW1, England **Place of chlormethiazole in treatment of alcoholics.** British Medical Journal (London). No. 6094:1088, 1977.

In a letter to the editor some remarks concerning the use of chlormethiazole for the treatment of severe alcohol withdrawal syndromes are presented to refute the view that its use in treating the depressed alcoholic ought to be avoided. Some of the risks of the indiscriminate use of chlormethiazole, including psychological and, more rarely, physical dependence, potentiation, and overdose, are mentioned, as are statistics on the presence of reactive depression in alcoholics during the alcohol withdrawal phase. 2 references.

001622 Iivanainen, M.; Viukari, M.; Helle, E.-P. Dept. of Neurology, University of Helsinki, Helsinki, Finland **Cerebellar atrophy in phenytoin-treated mentally retarded epileptics.** Epilepsia. 18(3):375-386, 1977.

The relationship among the serum concentration of phenytoin, pneumoencephalographic measurements describing cerebellar atrophy, and various other clinical variables was analyzed statistically in a series of 131 phenytoin treated mentally retarded epileptics. Results show that phenytoin levels in serum correlated significantly with the heights of the fourth ventricle suggests that an overdosage of phenytoin or an underlying disease, or both, were the probable causes of cerebellar impairment and atrophy. Brain-damaged mentally retarded epileptics appear to be unusually susceptible to the side-effects of phenytoin. 38 references.

001623 Mallach, H. J.; Raff, G.; Kraemer, R. Institute of Forensic Medicine, University of Tuebingen, Nagelestrasse 5, D-7400 Tuebingen, Germany **On the influence of Mobiletten on the effect of alcohol in the human: second communication: influence on the efficiency under alcohol stress.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 15(12):576-580, 1977.

The influence of alcohol in combination with the preparation Mobiletten on the psychophysical efficiency was studied in 15 probands using a variety of test methods. Under the combined influence of alcohol and Mobiletten the probands showed significantly less efficiency loss in regard to single test parameters than under alcohol without intake of Mobiletten. These changes were noted in a comparison of the test results obtained at respective points of time as well as those obtained when the blood ethanol concentrations were practically identical. The reduced increase rate of blood ethanol levels is suggested as a cause for these changes. However, any specific sobering effect of the preparation could not be demonstrated. 4 references. (Author abstract modified)

001624 Rabey, J. M.; Vardi, J.; Askenazi, J. J.; Streifler, M. Department of Neurology, Ichilov Hospital, Tel Aviv Municipal Governmental Medical Center, Tel Aviv, Israel **L-tryptophan administration in L-dopa-induced hallucinations in elderly Parkinsonian patients.** Gerontology (Basel). 23(6):438-444, 1977.

L-tryptophan (LT) was administered to eight elderly Parkinsonian patients who developed visual hallucinations with paranoidal features under L-dopa treatment in combination with alpha-methyldopa-hydrazine. Each patient's mental state was evaluated by a physician twice daily during one month hospitalization period, and daily record kept by nurse and family reports about physical and mental condition. In six patients LT ameliorated the symtomatology by arresting the visual paranoidal hallucinations or diminishing their frequency and relieving the psychomotor agitation. As a side-effect LT produced new pleasurable, LSD like visual images in three patients. In two patients, in whom LT did not affect the mental disturbances, amelioration was obtained only by phenothiazines. Theoretical considerations on dopamine, 5 role in the genesis of visual hallucinations and mental disturbances emphasizes the benefit of LT administration in this biopsychological syndrome. 27 references. (Journal abstract modified)

001625 Shouse, Margaret N.; Lubar, Joel F. V.A. Hospital, Sepulveda, CA 91343 **Management of the hyperkinetic syndrome with methylphenidate and SMR biofeedback training.** Biofeedback and Self-Regulation. 2(3):290, 1977.

In a paper read at the 5th annual meeting of the Biofeedback Society of America, Orlando, FL, March 1977, the management of the hyperkinetic syndrome with methylphenidate and sensory motor rhythm (SMR) biofeedback training was investigated. The effect of methylphenidate (Ritalin) was compared with SMR feedback training (12 to 14Hz) combined with inhibition of the feedback for lower frequencies (4 to 7Hz) in four severely hyperkinetic children with reduced physiological arousal. Following SMR training under Ritalin, the contingencies were reversed, and after several months the original contingencies were reintroduced. Finally, medication was withdrawn and SMR training alone was employed. Reversal of the contingencies led to increased hyperkinesis. Final SMR training following reversal led to marked improvement, which was fully maintained after Ritalin withdrawal.

001626 Stotsky, Bernard A. St. Elizabeth's Hospital of Boston, 736 Cambridge St., Boston, MA 02135 **Relative efficacy of parenteral haloperidol and thiothixene for the emergency treatment of acutely excited and agitated patients.** Diseases of the Nervous System. 38(12):967-970, 973, 1977.

A double-blind study of the relative efficacy of parenteral haloperidol and thiothixene for the emergency treatment of acutely excited and agitated patients is reported. Haloperidol (n=15) and thiothixene (n=15), administered parenterally in emergency rooms and outpatient facilities to 30 acutely excited, agitated psychotic patients in hourly doses of 4mg. or 8mg.,as needed over a 4 hour period, achieved rapid tranquilization in all 30 patients. Significant improvement was shown over a 6 hour period on total score, the four factors (thinking disorder, anergic state, excitement and disorientation, and depression), and also on hourly ratings of 17 symptoms of a Psychiatric Target Symptom Profile. No significant differences were found between the haloperidol treated and thiothixene treated groups. Few adverse reactions were noted, and all of them mild, the most frequent being drowsiness in six patients. (Journal abstract modified)

001627 Toaff, M. E.; Hezroni, J.; Toaff, R. Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel **Effects of diazepam on uterine activity during labor.** Israel Journal of Medical Sciences (Jerusalem). 13(10):1007-1012, 1977.

The effect of diazepam on uterine activity was assessed in a series of 30 patients in established spontaneous labor. The action of diazepam on the frequency and amplitude of contractions, uterine tone and fetal heartrate was monitored internally. An i.v. dose of 10mg diazepam significantly decreased uterine activity by its direct effect on contraction frequency. No effect on uterine tone was seen. This effect of diazepam on contraction frequency was additional to its tranquilizing and muscle relaxant action. 17 references. (Author abstract)

001628 Twycross, Robert. Churchill Hospital, Headington, Oxford, England **Value of cocaine in opiate-containing elixirs.** British Medical Journal (London). No. 6098:1348, 1977.

In a letter to the editor, the value of adding cocaine to opiate containing elixirs to relieve pain was discussed. A randomized controlled trial of morphine and diamorphine elixirs with and without cocaine was administered to 400 terminally ill patients on an individually determined regimen. Although introducing cocaine resulted in a small statistically significant increase in alertness, stopping cocaine had no detectable effect. It is concluded that the use of cocaine is questionable in light of its side-effects which sometimes includes depression. 5 references.

001629 Viukari, Matti; Linnoila, Markku. Koskela Geriatric Hospital, 00600 Helsinki 60, Finland **Effect of fusaric acid on tardive dyskinesia and mental state in psychogeriatric patients: a pilot study.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(1):57-61, 1977.

The effect of fusaric acid 150 to 450mg daily on tardive dyskinesia and mental state was studied in 15 chronic psychogeriatric patients. The patients' previous drug treatment was maintained unchanged during the experiment. Fusaric acid significantly relieved orofacial dyskinesia, tremor, and rigidity, and it improved the mental state of the patients (BPRS). Akathisia was exacerbated, but this change was not significant. Akinesia and anxiety were not altered. 17 references. (Author abstract)

001630 Yaryura-Tobias, J. A.; Neziroglu, F. A. North Nassau Mental Health Center, 1691 Northern Blvd., Manhasset, L.I., NY 11030 **Gilles de la Tourette syndrome: a new clinico-therapeutic approach.** Progress in Neuro-Psychopharmacology. 1(3/4):335-338, 1977.

Data on clinical aspects of the Gilles de la Tourette syndrome and the therapeutic effectiveness of chlorimipramine are reported. Self-ratings, clinical evaluation and family interviews of 20 patients revealed aggression and obsessive-compulsiveness as additional psychiatric symptoms of the syndrome. The presence of siblings having Tourette and obsessive-compulsiveness and/or tics in family members suggested a genetic trait. Doses of chlorimipramine (CLI, 25 to 350mg), a potent serotonergic blocking agent, in 15 patients, indicated good efficacy and control of 80 to 90% of the symptoms. CLI displayed the advantage over haloperidol of having milder side-effects. Findings of low manganese and CLI action on serotonin metabolism are taken to suggest serotonin disturbances as a causative factor in Tourette syndrome. 27 references.

12 PSYCHOTOMIMETIC EVALUATION STUDIES

001631 Barker, E. T.; Buck, M. F. Mental Health Centre, Penetanguishene, Ontario, Canada **LSD in a coercive milieu therapy program.** Canadian Psychiatric Association Journal (Ottawa). 22(6):311-314, 1977.

The use of LSD in a coercive milieu therapy program is described. Over a five year period, 30 patients in a maximum security mental hospital were treated with LSD. After undergoing the LSD experience each subject participated in an interview. Three different styles of interviewing procedure evolved with experience: 1) a medical model; 2) a "responsible street model;" and 3) a nondirective model. Although all patients reported that the experience was of great benefit, changes for better or worse were not observed by others. Chromosomal studies showed increased frequency of breaks. It was not thought that the LSD administration in the hospital was a significant factor leading to use of street drugs after release. The only difference in administration to psychopaths and schizophrenics was that one third of the psychopaths acted out by punching or kicking someone nearby. It is concluded that when used with safeguards, LSD can be a safe and valuable drug to use in communities of long-term patients because of the high morale engendered by it. 9 references. (Author abstract modified)

001632 Carter, Michael. no address **Why ban hallucinogens?** World Medicine (London). 12(19):51-52, 1977.

Implications of the banning of hallucinogens in England under the Misuse of Drugs Act of 1971 are discussed. Regulatory bodies have used information on abuse of hallucinogens to judge their usefulness, making human research with hallucinogenic drugs like LSD impossible. Generically based legislation (e.g. any derivative of amphetamine on which hallucinogens are based is to be restricted), which includes a few drugs found to exhibit no hallucinogenic properties, has crippled research into possible therapeutic applications. Though animal research continues, use of hallucinogens in studies of neurosis and schizophrenia, uniquely human conditions, are impossible. The spectrum of effects produced by hallucinogens is considered valuable for exploring sensory perception, thought processes, and emotional states and how they are integrated in the normal human personality. Possible psychotherapeutic applications, unique research protocols necessary with hallucinogens, and the need for more specific information on adverse effects (e.g. toxicity and behavioral disruption) are briefly discussed.

001633 Dew, Joseph M. Department of Family Practice, University of Louisville School of Medicine, Louisville, KY 40208 **Toxic delirium induced by deliberate ingestion of Jimson weed.** Journal of the Kentucky Medical Association. 75(9):434-436, 1977.

The physiology and pharmacology of Jimson weed (Datura stramonium) are discussed; physical presentation and emergency management of toxic delirium induced by ingestion of Jimson weed is reviewed; and an illustrative case report is presented. Atropinic/antimuscarinic drugs inhibit acetylcholine action and produce central nervous system excitation. Jimson weed is the most abundant source of scopalamine and atropine in the United States, and incidence of Jimson weed poisoning is increasing. Clinical presentation may include dry mouth and skin, dilated and nonreactive pupils, blurred vision, mental disorientation or excitement, fever, hallucinations, ataxia, memory impairment, depression, coma, and death. Physostigmine is of utility both in the diagnosis and treatment of Jimson weed induced anticholinergic toxicity. Repeated administration for a 12 to 24 hour period may be necessary. A detailed case report of Jimson weed toxicity in a 15-year-old male is presented. 16 references.

001634 Maykut, M. O. Non-Medical Use of Drugs Directorate, Room 850, Journal Building, 365 Laurier Ave. West, Ottawa, Ontario K1A 1B6, Canada **Pharmacotherapy of narcotic dependence.** Progress in Neuro-Psychopharmacology (Oxford). 1(1/2):31-49, 1977.

Medical management of narcotic dependence is discussed in terms of etiology, clinical syndrome, diagnosis, and specific treatment including methadone preparations and narcotic antagonists. Narcotic antagonists may prove to be useful in prevention, diagnosis, treatment, and rehabilitation of opiate dependence. The pharmacological actions of pure and partial antagonists are presented noting the differential properties that have practical application in helping to control opiate dependence and even prevent the development of a potential narcotic addict. The partial antagonists considered are divided into three classes: 1) those which are morphinelike with euphoric and addicting properties (profadol, propiram); 2) those that produce dysphoria (nalorphine, cyclacozine, levallorphan, oxilorphan, cyclorphan); and 3) those that have both euphoric and dysphoric or mixed effects (pentazocine). The pure antagonists discussed include naloxone and naltrexone. 55 references. (Author abstract modified)

001635 Mitrani, L.; Shekerdjiiski, S.; Gourevitch, A.; Yanev, S. Institute of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria **Identification of short time intervals under LSD25 and mescaline.** Activitas Nervosa Superior (Praha). 19(2):103-104, 1977.

The effects of LSD25 and mescaline on the identification of time intervals of up to 2 seconds were studied in six volunteer subjects. Mescaline and LSD25 did not affect the ability to identify short time intervals given by light stimulation of different duration. An ambiguous situation was seen to arise in which the subjective feelings of changes in the time course under mescaline and LSD25 were in contradiction with the results of the measurements on short time interval identification, which suggests two mechanisms of time interval identification which might act independently. 4 references.

001636 Muller, Diethard. Nervenklinik der Medizinischen Akademie, Leipziger Strasse, 44, DDR-3000 Magdeburg, Germany **/Neurophysiological parameters of droperidol induced psychoses./** Neurophysiologische Parameter bei droperidolinduzierten Psychosen. Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 29(4):210-215, 1977.

Neurophysiological aspects of psychoses induced by high doses of droperidol are reported. Twelve normal subjects, 16 to 64 years old, were given 140mg to 200mg droperidol and psychopathological effects (temporary hallucinatory syndrome), EEG (distinct posterior theta groups), EMG and electroneurographic results (H-amplitude depression), as well as ECG results (tachycardia, extrasystoles) are discussed with reference to possible mechanisms of action. Whether the psychopathological symptoms are related to the drug's effects on the brainstem remains to be resolved. 13 references. (Journal abstract modified)

001637 Showalter, Craig V.; Thornton, William E. Substance Abuse Services, Inc., 1439 South Michigan Ave., Chicago, IL 60605 **Clinical pharmacology of phencyclidine toxicity.** American Journal of Psychiatry. 134(11):1234-1238, 1977.

The clinical pharmacology of the toxicity of phencyclidine, a psychedelic drug, is reviewed, with attention to the sensory, psychological, and behavioral symptoms of intoxication. Phencyclidine appears to be unique in action compared with other psychedelic drugs, and its effects are less dependent upon the individual's personality than are the effects of LSD or mescaline. Most cases of intoxication are of short duration and the only treatment necessary may be observation together with minimal stimulation and diazepam. However, prolonged and severe behavioral disturbances, exaggeration of preexisting thought disorder, and serious medical complications commonly occur and must be considered in the treatment plan. 38 references. (Author abstract modified)

001638 Szulc, Tad. no address **/CIA research with LSD-25./** The CIA's electric kool-aid acid test. Psychology Today. 11(6):92-94, 97, 101-104, 151, 153, 1977.

The experimentation of the U.S. Central Intelligence Agency (CIA) with LSD25 and other means of behavioral control or brainwashing for over 25 years, is reviewed in the context of the Cold War climate that produced the program. The ethical issues involved in the often deceptive research are discussed. The program was conducted at a cost of at least $25 million at 86 U.S. and Canadian hospitals, prisons, universities, and military installations, as well as the agency's own "safe houses" in Washington, New York, and San Francisco. The research program is adjudged to have been in violation of U.S. law,

Nuremburg convention, and the ethical standards of the various scientific professions involved.

001639 Villoldo, Alberto. P.O. Box 84, Cotati, CA 94928 **An introduction to the psychedelic psychotherapy of Salvador Roquet.** Journal of Humanistic Psychology. 17(4):45-58, 1977.

The use by Dr. Salvador Roquet of psychedelic drugs as key tools of a synthesis oriented therapeutic process to complement with exactness the evolving needs of the patient is described. Two therapies used by Roquet are described as well as a sample psychodysleptic session. Roquet claims to have obtained with psychosynthesis the results expected from long-term psychoanalysis in an abbreviated period of time. It is suggested that while psychedelic therapy may prove valuable, the technique has not proved useful in resolving therapeutic issues which provide support for the development of new and more dynamic personality structures. 10 references.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

001640 Abraham, Donald J. Dept. of Medicinal Chemistry, Univ. of Pittsburgh, Pittsburgh, PA 15261 **Addendum concerning a proposed model for the action of lithium.** Communications in Psychopharmacology. 1(6):611, 1977.

A proposed theory for the action of lithium is brought into question by equivocal results in a replication. The proponent of the theory reports that a new coworker using the identical procedures published in Communications in Psychopharmacology 1, 363 (1977) except for the use of a superiorly designed tonometer, could not reproduce the effect of lithium on hemoglobin oxygen equilibrium curves with 2,3-diphosphoglyceric acid, i.e. no shift in the DPG curve toward stripped hemoglobin in the presence of lithium. It is noted that without this finding, the theory should be held suspect, and apologies are made to trusting colleagues. 1 reference. (Author abstract modified)

001641 Baldessarini, Ross J. Chief, Laboratory of Neuropharmacology, Massachusetts General Hospital, Boston, Massachusetts, USA **/Development and application of methods for determining the biological transmethiolations dependent on S-Adenosyl-L-Methionine./** Svilupo ed applicazione dei metodi per la determinazione delle transmetilazioni biologiche S-adenosilmetionina dipendenti. In: Baldessarini R. Transmetilazioni e sistema nervoso centrale. Rome, Minerva Medica, 1976. p. 51-74.

The development and application of different methods for determining the effect of methionine, associated with other aminoacids, on schizophrenics and other mentally ill subjects are discussed and evaluated on the basis of recent clinical experiments with animals and humans. A review of recent research shows that methionine used with the mentally ill can increase the availability of S-adenosylmethionine (SAMe) needed for transmethiolation of biogenic amines. From present data available it appears that methionine does increase biogenic amine methiolation, but the hypothesis that methionine exacerbates psychotic symptomatology in schizophrenics cannot be supported at this time due to the paucity of clinical research on SAMe in humans. 99 references.

001642 Ban, Thomas A.; Amin, Mohammed; Lehmann, Heinz E. Vanderbilt University, Nashville, TN 37240 **Clinical studies with maprotiline and the reversed catecholamine hypothesis of depression.** Current Therapeutic Research. 22(6):886-893, 1977.

The reversed catecholamine hypothesis of depression, which states that depression is associated with a relative deficiency of norepinephrine (NE) at functionally important central adrenergic sites, was investigated in a 26 week uncontrolled open clinical trial with maprotiline, a tetracyclic antidepressant. It was speculated that the reversed catecholamine hypothesis of depression would be supported if maprotiline resulted in a biphasic therapeutic response curve in time, i.e. increase in depressive psychopathology associated with increase in available catecholamines immediately after therapy, followed by decrease in depressive psychopathology and a decrease in catecholamines and possible a decrease in urinary concentration of 3-methoxy-4-hydroxyphenylglycol, a metabolite of NE. Results show that the proposed biphasic therapeutic response curve in time was not present after treatment with maprotiline, thereby disproving the reversed catecholamine hypothesis. 9 references. (Author abstract modified)

001643 Benowitz, Neal L.; Jones, Reese T. Langley Porter Neuropsychiatric Institute, University of California, San Francisco, CA 94143 **Effects of delta9-tetrahydocannabinol on drug distribution and metabolism: antipyrene, pentobarbital, and ethanol.** Clinical Pharmacology and Therapeutics. 22(3):259-268, 1977.

The effects of delta9-tetrahydrocannabinol (THC) ingestion on the metabolism of antipyrene and pentobarbitol that are metabolized by microsomal enzymes were investigated as well as its interactions with ethanol, which is ofen used with cannabis. Twenty two hospitalized healthy volunteer subjects received THC, 60 to 180mg/day in divided doses for 14 days. Bodyweight increased and plasma proteins decreased in all subjects. Total bilirubin was significantly lower, while other liver function tests remained normal. A within subject comparison of the pharmacokinetics of antipyrine, pentobarbital, or ethanol given before, during, and after THC was performed. The effect of THC on disappearance rate of these drugs appeared to be due to a combination of: 1) increased distribution volume, due in part to expansion of extracellular fluid volume noted during THC ingestion; and 2) diminished metabolic clearance. THC also delayed absorption of pentobarbital and ethanol in several subjects. It is suggested that the effects of THC on absorption and drug elimination must be considered in evaluating interaction with other drugs. 34 references. (Journal abstract modified)

001644 Birch, N. J.; Greenfield, A. A.; Hullin, R. P. Dept. of Biochemistry, Univ. of Leeds, 9 Hyde Terrace, Leeds LS2 9L5, England **Lithium therapy and alkaline earth metal metabolism: a biochemical screening study.** Psychological Medicine (London). 7(4):613-618, 1977.

Ninety patients receiving lithium prophylactically for recurrent affective disorder were investigated in a biochemical screening study of lithium therapy and alkaline earth metal metabolism. A total of 90 biochemical variables were analyzed by correlation matrices. Results indicate no major changes in urinary excretion of calcium and magnesium during long-term lithium therapy, although it is cautioned that this finding may reflect the insensitivity of the screening technique used. However, it is concluded that the high correlation between urine excretion rates indicates that this "spot" technique may be useful for a large group of subjects. 37 references. (Author abstract modified)

001645 Braestrup, C.; Albrechtsen, R.; Squires, R. F. Psychopharmacological Research Laboratory, Dept. E., DK-4000 Roskilde, Denmark **High densities of benzodiazepine recep-**

tors in human cortical areas. Nature (London). 269(5630):702-704, 1977.

An in vitro investigation of benzodiazepine receptor density in human cortical areas is reported in a letter to the editor. Crude synaptosomal preparations of human brain tissue were incubated for 40 min with (3H)diazepam and regional distribution and densities of binding sites were assessed. Regional distribution was similar in all four brains studied: frontal cortex, occipital cortex, cerebellar cortex, temporal cortex, and hippocampus showed the highest densities of specific binding sites; corpus striatum, globus pallidus, and hypothalamus showed intermediate densities; and low densities were found in corpus callosum, nucleus dentatus, and pons. Results suggest that cortical areas, as well as hippocampus may be important for the action of benzodiazepines. Similarities in regional distribution and affinity constants in rat and human brain are noted. 20 references.

001646 Chapman, C. Richard; Benedetti, Costantino. Dept. of Anesthesiology, University of Washington School of Medicine, Seattle, WA **Analgesia following transcutaneous electrical stimulation and its partial reversal by a narcotic antagonist.** Life Sciences (Oxford). 21(11):1645-1648, 1977.

The effects of transcutaneous electrical stimulation on the perception of pain in human subjects and the analgesic action of naloxone on this perception were investigated. Transcutaneous electrical stimulation was employed at two sites in the second trigeminal division to induce dental analgesia in 24 human subjects who were undergoing painful tooth pulp stimulation. Injection of either 1ml (0.4mg) naloxone or 1ml saline was given to each volunteer after 20 minutes of stimulation under double-blind conditions. Saline subjects showed no loss of analgesia, while naloxone subjects had a partial and significant loss of analgesia. This observation suggests that endogenic opiate like substances play a role in stimulation induced analgesia. 9 references. (Author abstract modified)

001647 Chun, A. H. C.; Carrigan, P. J.; Hoffman, D. J.; Kershner, R. P.; Stuart, J. D. Abbott Laboratories, North Chicago, IL 60064 **Effect of antacids on absorption of clorazepate.** Clinical Pharmacology and Therapeutics. 22(3):329-335, 1977.

The effect of a magnesia and alumina antacid suspension on the absorption of clorazepate dipotassium was studied in 15 normal healthy adult subjects who ingested a 15mg dose of clorazepate alone or with single or multiple doses of antacid. The results of this three period randomized complete crossover study showed a trend of initially slower suspension. However, there were no significant differences among treatments in the extent of absorption as measured by the area under the plasma level time curves. Clorazepate plasma levels were of relatively short duration and similar for all treatments. The urinary excretion pattern was likewise comparable with conjugated oxazepam, the major species measured. Plasma elimination half-lives of nordiazepam and clorazepate were not affected by the antacid treatments. 13 references. (Journal abstract modified)

001648 Chweh, Andrew Y.; Pulsinelli, Phillip D.; Goehl, Thomas J.; Abraham, Donald J.; Miklos, Francis; Draus, Frank; Mallinger, Alan G. Dept. of Medicinal Chemistry, School of Pharmacy, Univ. of Pittsburgh, Pittsburgh, PA 15261 **A proposed model for the action of lithium.** Communications in Psychopharmacology. 1(4):363-372, 1977.

A model is proposed for the action of lithium (Li) in red blood cells in terms of the effect of Li+ on the allosteric effector 2,3-diphosphoglyceric acid (DPG) and its regulatory interaction with human hemoglobin (Hb). It was found that Li+ substantially disrupts DPG's ability to bind to or stabilize the deoxy form (T-state) of Hb, thus resulting in a shift in the allosteric equilibrium more towards the high affinity oxy form (R-state), during oxygenation reactions. Increased intracellular Li+, its competitive interaction with DPG, the subsequent decreased availability of oxygen for brain biochemical processes, and the possible implications related to lithium's use in the treatment of mania are discussed. 20 references. (Author abstract)

001649 Clark, Mervin L.; Paredes, Alfonso; Costiloe, J. Paul; Wood, Fredda. Central State Griffin Memorial Hospital, P.O. Box 151, Norman, OK 73070 **Evaluation of butaclamol in chronic schizophrenic patients.** Journal of Clinical Pharmacology. 17(8,9):529-536, 1977.

Butaclamol was evaluated in 27 chronic male and female schizophrenic patients, 21 to 65 years old, who had been institutionalized for at least 2 years, in a 4 week double-blind, placebo controlled trial using chlorpromazine as the standard drug of comparison. Butaclamol (50mg/day) had significant antipsychotic activity comparable to chlorpromazine, but with a much higher incidence of extrapyramidal signs. Rebound insomnia also was observed. It is suggested that future studies aim at daily doses lower than 50mg. 7 references.

001650 Cleghorn, R. A. Department of Psychiatry, McGill University Faculty of Medicine, Montreal, Quebec, Canada **Morphine-like peptides of brain and their relation to hormonal neurotransmitters.** Psychiatric Journal of the University of Ottawa (Ottawa). 2(3):133-137, 1977.

Morphine-like peptides of the brain, endorphins and enkephalins, and their relation to hormonal neurotransmitters are described in a review of recent neurological research. Among peptides produced in the hypothalamus are some which have been shown to act on spontaneous electrical energy of the brain, to affect behavior in depression, and to affect conditioning behavior by producing persistence of memory of the conditioning process. A critical contributing concept to the understanding of the effect of opiates was the finding that there is a relationship between drug action of agents derived from nature and counterparts within the body. Since the central nervous system itself is too complex, morphine sensitive structures in the peripheral autonomous nervous system were studied. Naturally occurring substances in animal brain were found to act like opiates and were called enkephalins. In other research, enkephalins were shown to modify the excitability of some neurons. The effect of opiates in humans is less a specific blunting of pain than a production of a state of indifference. It has been postulated that endorphins play a central role in the control of affective states, and that narcotic addiction could be an endorphin deficiency. 17 references.

001651 Conney, A. H.; Pantuck, E. J.; Kuntzman, R.; Kappas, A.; Anderson, K. E.; Alvares, A. P. Department of Biochemistry and Drug Metabolism, Hoffman-LaRoche, Inc., Nutley, NJ 07110 **Nutrition and chemical biotransformations in man.** Clinical Pharmacology and Therapeutics. 22(5,Part 2):707-720, 1977.

A review of research in man and in animals is presented to elucidate the importance of nutritional factors in the regulation of drug metabolism. Studies of dietary carbohydrate/protein ratios indicate that high protein and low carbohydrate intake

increases rates of metabolism for antipyrine and theophylline, while a low protein/high carbohydrate diet decreases metabolism to the home diet baseline rate. Another series of studies indicated that polycyclic aromatic hydrocarbons act as inducers of drug metabolizing enzymes. Further dietary studies indicated marked individual differences in metabolic responses to dietary alterations. Feeding Brussels sprouts or cabbage to rats also enhanced the intestinal metabolism of 7-ethoxycoumarin, benzo(a)pyrene, and hexobarbital. Pretreatment of rats with several indoles that are present in cabbage and Brussels sprouts stimulated the intestinal metabolism of phenacetin, 7-ethoxycoumarin, benzo(a)pyrene, and hexobarbital. Additional studies are needed to more fully explore the effects of dietary factors on the action of drugs, environmental pollutants, and normal body constituents in humans. 54 references. (Author abstract modified)

001652 D'Elia, G.; Lehmann, J.; Raotma, H. no address **Evaluation of the combination of tryptophan and ECT in the treatment of depression: 2. Biochemical analysis.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(4):319-334, 1977.

Serum levels of total L-tryptophan (L-TP) were determined in patients suffering from endogenous depression, randomly assigned to two groups, one treated with L-TP (6g daily) and unilateral ECT, the other with placebo and unilateral ECT. The degree of amelioration in depressive symptomatology was measured by doctors', nurses', and patients' rating scales. The levels of L-TP during the treatment with L-TP and ECT showed no relationship to residual symptomatology after the treatment. Thus the L-TP levels do not seem to have a therapeutic significance when treating depressed patients with ECT. 104 references. (Author abstract modified)

001653 Davis, Kenneth L.; Hollister, Leo E.; Goodwin, Frederick K.; Gordon, Edna K. Stanford School of Medicine, Palo Alto, CA 94304 **Neurotransmitter metabolites in the cerebrospinal fluid of man following physostigmine.** Life Sciences (Oxford). 21(7):933-936, 1977.

The effect of physostigmine on brain dopamine, norepinephrine, and serotonin was investigated by administering the drug to 23 normal subjects and assaying their cerebrospinal fluid. A 3.0mg dose of physostigmine or normal saline was given intravenously to the subjects who had been treated with probenecid. Homovanillic acid and 3-methoxy-4-hydroxyphenylglycol concentrations were significantly higher in the lumbar cerebrospinal fluid of subjects who received physostigmine than subjects who received normal saline. This establishes biochemical evidence for a cholinergic link in the central nervous system of man. 34 references. (Journal abstract)

001654 De Leon-Jones, Frank A.; Pandey, Ghanshyam N.; Davis, John M.; Garver, David L.; Inwang, Edet E. VA West Side Hospital, PO Box 8195, Chicago, IL 60680 **Urinary cyclic AMP excretion by methadone subjects during gradual and acute withdrawal.** Psychopharmacology (Berlin). 54(1):17-20, 1977.

The behavior of cyclic adenosine monophosphate (cyclic AMP) levels during tolerance to narcotic drugs and withdrawal was investigated. Serial 24 hour urinary excretion of cyclic AMP by 27 long-term methadone addicts was determined during a period of stable methadone intake, a period of gradual withdrawal, and a period of acute withdrawal. Cyclic AMP excretion during stable methadone intake was identical to that of normal control subjects. Neither gradual nor acute withdrawal appeared to affect the urinary excretion of cyclic AMP. The data agree with previous reports in the literature which suggest that cyclic AMP levels are not altered during tolerance to narcotics, but do not support the hypothesis that levels of the nucleotide might be increased during withdrawal. 23 references. (Author abstract modified)

001655 Eberts, F. S., Jr.; Philopoulos, Y.; Reineke, L. M.; Vliek, R. W.; Metzler, C. M. Upjohn Co., Kalamazoo, MI 49001 **Disposition of ketazolam, a new anxiolytic agent, in man.** Pharmacologist. 19(2):165, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the disposition of ketazolam (K), an anxiolytic agent, in humans was reported. After administration of K, the mean peak plasma levels of K and some of its metabolites were determined. Diazepam (D), N-demethylketazolam (DK), N-demethyldiazepam (DD) were major metabolites. The plasma half-life of K was 1.5hr, that of D was 28 hr, and that of DK/DD was 50 hr. K was rapidly demethylated to DK resulting in a plasma DK/DD levels ten times greater than K plus D levels; this contrasts sharply with levels of D being greater than that of DD reported after D administration. Radioactivity was slowly excreted in urine (80%) and feces (20%). The major urinary metabolite of K was oxazepam, predominantly in conjugated form. Smaller amounts of D and DD were found in urine and feces. Feces contained less than 1% of the dose as K or D, indicating good absorption of the formulation. (Author abstract modified)

001656 Finkle, Bryan Smith. University of Utah, Salt Lake City, UT **The metabolism and plasma concentrations of L-alpha-acetylmethadol and its metabolites in man. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-23104 HC$15.00 MF$7.50 279 p.

To determine the plasma disposition of L-alpha-acetylmethadol (LAAM) and its active metabolites, norLAAM and dinorLAAM, LAAM was administered to 12 human subjects orally three times per week for ten doses ranging between .73mg/kg to 1.51mg/kg. A new quantitative, specific, and extremely sensitive analytical method was developed which is reported in detail. Maximum plasma concentrations after the first dose of LAAM varied from 52 to 510ng/ml (mean time 4.4hr) for LAAM, 65 to 175ng/ml (5.6hr) for norLAAM, and 11 to 92ng/ml (6.6hr) for dinorLAAM. Three subjects continuously accumulated LAAM and its metabolites, two accumulated LAAM alone, and one accumulated dinorLAAM alone; the remaining subjects reached plateau concentrations after the 4 to 5 hour half-lives anticipated. Maximum plasma concentrations increased over the ten dose period by a factor of 2.0for LAAM, 2.0to 4.0for norLAAM, and 4.0to 10.0for dinorLAAM. Plasma concentration/time/course profiles are generally consistent with a two compartment, first order kinetic model. (Journal abstract modified)

001657 Finley, William W. Research Psychology Department, Children's Medical Center, PO Box 35648, Tulsa, OK 74135 **Effects of mysoline and dilantin on the EEG during SMR biofeedback training of a psychomotor epiletic: single case study.** Biofeedback and Self-Regulation. 2(3):286, 1977.

In a paper read at the 5th annual meeting of the Biofeedback Society of America, Orlando, FL, March 1977, the effects of mysoline and dilantin on the EEG during sensory motor rhythm (SMR) biofeedback training of a psychomotor epileptic were investigated. Analysis of the results of training to augment 12Hz activity showed a significant increase in SMR production with a concomitant suppression of seizure events (auras and seizures). Observation of the anticonvulsant

medication showed that high levels of Mysoline were associated with low percent SMR production. Following complete withdrawal of Mysoline, percent SMR abruptly increased. No significant relationship between plasma levels of Dilantin and percent SMR was found.

001658 Frazer, Alan; Mendels, Joe; Brunswick, David. Veterans Administration Hospital, Philadelphia, PA 19104 **Transfer of lithium ions across the erythrocyte membrane.** Communications in Psychopharmacology. 1(3):255-270, 1977.

Mechanisms involved in the transfer of the lithium ion (Li+) across the erythrocyte (RBC) membrane were explored. Isolated erythrocytes were incubated in vitro at 37 degrees under different experimental conditions, and either the uptake of Li+ into the cell or the efflux of the cation from the cell was measured. The presence of sodium ions in the incubation medium had a dual effect: 1) reducing the net accumulation of Li+ by erythrocytes; but 2) accelerating the rate of loss of Li+ from erythrocytes. Ouabain produced an increase in the net accumulation of Li+ by erythrocytes only if there was a rise in cell Na+. Furosemide did not affect the transfer of Li+ across the erythrocyte membrane, whereas phloretin did reduce net Li+ accumulation. 24 references. (Journal abstract)

001659 Friedhoff, Arnold J. Millhauser Laboratories, NYU School of Medicine, 550 1st Avenue, New York, NY 10016 **Receptor sensitivity modification (RSM) -- a new paradigm for the potential treatment of some hormonal and transmitter disturbances.** Comprehensive Psychiatry. 18(4):309-317, 1977.

A paradigm of receptor sensitivity modification (RSM), which has potential for the treatment of some hormonal and transmitter disturbances, is hypothesized and tested. The model proposes: 1) that receptor cells can change receptor setpoint, either increasing or decreasing the sensitivity; 2) that these changes occur in the direction of restoring homeostasis; 3) that these processes proceed with a slower time course than the phasic nervous activity; 4) that the adaptive processes must be under active regulatory control; and 5) that persistent change in sensitivity reflect an enduring change in regulatory processes in the cell. A case study of tardive dyskinesia, which is described, indicates that doses of l-dopa can successfully treat this sypmtom and thus supports the idea that receptor sensitivity can be modified. The possible application of this principle of RSM for the treatment of schizophrenia is discussed. 26 references.

001660 Galt, R. H. B. Imperial Chemical Industries Ltd., Pharmaceuticals Division, Mereside, Alderley Park, Macclesfield, Cheshire, England **The opiate anomalies -- another possible explanation?** Journal of Pharmacy and Pharmacology (London). 29(11):711-714, 1977.

Anomalies appearing in the structure and function of opiates are summarized in light of current knowledge, and alternative explanations are examined. Models of the morphine receptor are presented and discussed, and it is pointed out that stereochemical abnormalities of opiates are often overlooked because they are not consistent with other known data. 22 references.

001661 Gold, M. S.; Donabedian, R. K.; Dillard, M., Jr.; Slobetz, F. W.; Riordan, C. E.; Kleber, H. D. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Antipsychotic effect of opiate agonists.** Lancet (London). No. 8034:398-399, 1977.

In a letter to the editor, the results of a study of the antipsychotic effects of the opiate agonists methadone, on serum prolactin are presented. Methadone was administered orally to seven male volunteers while seven controls received colored water. Methadone was found to produce a significant rise in serum prolactin; there were no significant changes in controls. Data suggest that methadone interferes with the postsynaptic action of dopamine. It is concluded that if opiate agonists are not antipsychotic in man, then inhibition of dopamine impulse flow or release as assessed in vivo by increases in serum prolactin may not be a viable model for the antipsychotic locus of action of the neuroleptics. 19 references.

001662 Greenblatt, David J.; Comer, Walter H.; Elliott, Henry W.; Shader, Richard I.; Knowles, John A.; Ruelius, Hans W. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Clinical pharmacokinetics of lorazepam. III. Intravenous injection. Preliminary results.** Journal of Clinical Pharmacology. 17(8,9):490-494, 1977.

Pharmacokinetic properties of 5mg lorazepam i.v. were studied in four healthy male volunteers. Concentrations of lorazepam and its glucuronide metabolite were determined in multiple venous blood samples drawn during the 48 hours after dosing and in all urine collected during 96 hours after the dose. Mean pharmacokinetic parameters for lorazepam were: apparent elimination half-life 13.2hours; volume distribution 0.84 liter/kg; and total clearance 55.3ml/min. Lorazepam glucuronide promptly appeared in the blood, reached peak levels within 6 hours after the dose, and then declined in parallel with lorazepam. A mean level of 69% of dose was recovered in urine as lorazepam glucuronide. The mean apparent half-life of urinary excretion of lorazepam glucuronide was 17.4hours. 22 references.

001663 Greenblatt, David J.; Harmatz, Jerold S.; Stanski, Donald R.; Shader, Richard I.; Franke, Kate; Koch-Weser, Jan. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Factors influencing blood concentrations of chlordiazepoxide: a use of multiple regression analysis.** Psychopharmacology (Berlin). 54(3):277-282, 1977.

In a study of factors influencing blood concentrations of chlordiazepoxide (CDX), three groups of male and female Ss, aged 24 years to 74 years, received chlordiazepoxide hydrochloride by mouth as a single dose or as two divided doses, and the relation of plasma or whole blood concentrations for CDX and its metabolite, desmethylchlordiazepoxide (DMCDX), to time since the last dose, weight, age and sex were determined by simple and multiple regression analyses. Both CDX and DMCDX levels were negatively correlated with weight. Concentrations of CDX decreased, while those of DMCDX increased, with the time since the last dose. Lower levels of both drugs were associated with female sex, and lower levels of DMCDX were noted with increasing age. In the largest sample group, age and weight were more important variables than sex in accounting for CDX and DMCDX. Sex was of significance, and more important than time or age in explaining the variance of CDX in one series of observations. Multiple regression analysis is a useful approach to assessing interrelated factors influencing blood levels of drugs, especially when combined with a consideration of the interactive components of variance. Age and sex, in addition to weight and time, may be important factors that deserve further attention. 17 references. (Author abstract modified)

001664 Greenblatt, David J.; Knowles, John A.; Comer, Walter H.; Shader, Richard I.; Harmatz, Jerold S.; Ruelius

Hans W. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Clinical pharmacokinetics of lorazepam. IV. Long-term oral administration.** Journal of Clinical Pharmacology. 17(8,9):495-500, 1977.

Steady state plasma concentrations of lorazepam were assessed during long-term p.o. therapy. Healthy male volunteers (n=15) were given up to 10mg/day lorazepam for 26 weeks. At a dose of 6mg/day, the mean steady state lorazepam plasma level was 88ng/ml, and the lorazepam glucuronide level was 170ng/ml. Mean levels for subjects (n=7) who received 10mg/day were 164ng/ml and 266ng/ml, respectively. Lorazepam concentrations fluctuated from week to week despite constant dosage. Lorazepam mean steady levels were highly correlated with daily dose in mg/kg, but were not related to age. Lorazepam was not detected in plasma samples drawn 1 week after discontinuation of treatment. 13 references.

001665 Greenblatt, David J.; Shader, Richard I.; Franke, Kate; MacLaughlin, Dean S.; Ransil, Bernard J.; Koch-Weser, Jan. Clinical Pharmacology Unit, Massachusetts General Hospital, Bosotn, MA 02114 **Kinetics of intravenous chlordiazepoxide: sex differences in drug distribution.** Clinical Pharmacology and Therapeutics. 22(6):893-903, 1977.

In a study of the kinetics of intravenous chlordiazepoxide, sex differences in drug distribution are reported. Fourteen healthy subjects (7 male and 7 female) received 50mg of chlordiazepoxide (CDX) hydrochloride by 1 hr intravenous infusion. Multiple venous blood samples drawn during the 72 hr after the infusion were assayed for whole blood concentrations of CDX and of its major metabolite, desmethylchlordiazepoxide (DMCDX). Mean pharmacokinetic parameters, determined by weighted nonlinear least-squares regression analysis, were: distribution half-life, elimination half-life, volume of central compartment (V1), total distribution space (Vd), and total clearance. V1 and Vd were significantly larger among females than among males suggesting more extensive drug distribution in females. Values of half-life and of clearance did not, however, differ significantly between sexes. A second study in three subjects compared simultaneous whole blood and plasma CDX concentrations after intravenous bolus injection and showed them to be highly correlated. Red cell/plasma partition ratios indicated limited uptake of CDX by red cells. Volumes of distribution and clearances calculated from CDX concentrations in whole blood are larger than those based on plasma concentrations. 44 references. (Author abstract modified)

001666 Kadouch, Rachel; Belmaker, Robert H.; Ebstein, Richard P.; Peres, Leon. Department of Research, Jerusalem Mental Health Center, Ezrat Nashim, POB 140, Jerusalem, Israel **The mood response and plasma cyclic-AMP response to intravenous methylphenidate.** Neuropsychobiology (Basel). 3(4):250-255, 1977.

To determine if a peripheral measure of receptor sensitivity could predict central mood effects of stimulants, the plasma cyclic adenosine monophosphate (AMP) response and the mood response to intravenous methylphenidate were determined simultaneously in 12 patients with depressed affect and one normal control. No correlation between the two responses was found. The results indicated no mean difference between the peak rise of plasma cyclic AMP of those subjects with marked, minimal or absent mood response to methylphenidate, no significant rank order correlation between the rises in plasma cyclic AMP and the ranking of the mood and activation responses by the observers, and no significant rank correlation between the systolic or diastolic blood pressure response to the methylphenidate infusion and the mood response or between the systolic or diastolic blood pressure response and the cyclic AMP response. 18 references. (Author abstract modified)

001667 Kennedy, K. A.; Halmi, K. A.; Fischer, L. J. Dept. of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Urinary excretion of a quaternary ammonium glucuronide metabolite of cyproheptadine in humans undergoing chronic drug therapy.** Life Sciences (Oxford). 21(12):1813-1819, 1977.

The urinary excretion of cyproheptadine glucuronide was studied during the first and third weeks of drug treatment in women undergoing chronic therapy for anorexia nervosa. An average of 24% of the daily cyproheptadine dose was excreted at a relatively constant rate as the quaternary ammonium glucuronide metabolite. No remarkable changes in the rate or extent of the urinary excretion of cyproheptadine glucuronide were found with continued drug treatment. The results indicate that formation of a quaternary ammonium glucuronide represents a quantitatively important pathway for elimination of cyproheptadine in humans. 11 references. (Author abstract)

001668 Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Clinical biochemical assessment of drug action in patients. (Unpublished paper).** Bethesda, MD, NIMH, 1977. 1 p.

The interaction between drugs and tissue components and the resultant changes in enzyme activity, metabolic or transport processes or levels of receptor activation or sensitivity is discussed. It is noted that such studies cannot be carried out on human subjects in the same manner as they can with experimental animals. Isotopic methods are suggested to assess metabolic rates in particular tissues or to study distribution and rates of metabolism of drugs. Current attempts at such assessments in humans or primates are discussed and possible directions of future research are indicated.

001669 Lahrichi, Mohamed; Houpert, Yves; Tarallo, Pierrette; Loppinet, Vincent; Siest, Gerard. Centre de Medecine Preventive, 2 avenue du Doyen Jacques Parisot, 54500 Vandoeuvre-les-Nancy, France **Protein and enzyme release from human leukocytes: influence of phenothiazine derivatives.** Chemico-Biological Interactions (Amsterdam). 19(2):173-183, 1977.

To examine the effects of chlorpromazine and other phenothiazine derivatives on protein and enzyme release from human leukocytes, isolated human granulocytes were incubated in mediums containing chlorpromazine or other phenothiazines and release of lactate, adenosine triphosphate, dihydroxyacetone phosphate, alpha-glycerol-1-phosphate, lactate dehydrogenase, pyruvate kinase, and beta-glucoronidase was assessed. Chlorpromazine had a biphasic effect on enzyme release and the inhibition of the glycolytic pathway could be demonstrated only at high concentrations of chlorpromazine, after one hour's incubation. The NAD+/NADH ratio was significantly perturbed at all the concentrations. This effect is time dependent. The action of four other phenothiazine derivatives made it possible to establish a relationship between their physicochemical properties and protein release. The results are compared with those from other studies using other biological materials. 37 references. (Author abstract modified)

001670 Linnoila, M.; Leppaluoto, J.; Seppala, T.; Ranta, T. Dept. of Pharmacology, University of Helsinki, Helsinki, Fin-

land **Serum gonadotropin and TSH levels after tricyclic antidepressants in healthy males.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(3):285-288, 1977.

In a letter to the editor, the effects of tricyclic antidepressants on serum gonadotropin and thyroid stimulating hormones (TSH) levels were investigated in 20 healthy male volunteers. Chlorimipramine, nortriptyline, and doxepin were all found to increase the levels of these hormones. It was not possible to determine whether the primary target of tricyclic antidepressant action is the hypothalamus or the pituitary gland. It is suggested that the resulting increase in hormonal levels might have psychotropic effects which would modify the effects of the tricyclic antidepressants. 6 references.

001671 Maas, James W. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **The effects of psychopharmacological agents on central nervous system amine metabolism in man.** Annual Review of Pharmacology and Toxicology. 17:411-424, 1977.

Studies on the effects of psychotropic drugs on central nervous system (CNS) amine metabolism in man are reviewed. The studies are grouped into the following categories: 1) the effect of antipsychotic drugs on dopamine and serotonin metabolism in the cerebrospinal fluid; 2) the effect of antidepressant drugs on CNS amine metabolism; and 3) the effect of lithium on CNS amine metabolism. The results which the administration of these drugs have on the levels of 3-methoxy-4-hydroxyphenethyleneglycol, homovanillic acid, and 5-hydroxyindoleacetic acid are reported, and the implications of these findings are discussed. 60 references.

001672 Mehl, E.; Ruther, E.; Redemann, J. Neurochemische Abteilung, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munchen 40, Germany **Endogenous ligands of a putative LSD-serotonin receptor in the cerebrospinal fluid: higher level of LSD-displacing factors (LDF) in unmedicated psychotic patients.** Psychopharmacology (Berlin). 54(1):9-16, 1977.

The effect of the level of LSD displacing factor (LDF) substanus present in human cerebrospinal fluid on psychotics' responses to antipsychotic drugs was investigated. The LDF concentration was assayed in the cerbrospinal fluid of 49 nonpsychotic and of 19 acute psychotic patients before therapy with the antipsychotic drugs haloperidol or clozapine. LDF concentration was found to be significantly higher in the group of unmedicated acute psychotic patients in comparison to the control group. Within this group of acute psychotic patients, a high positive correlation was found between concentration of LDF and clinical improvement. Thus, a nosological subgroup was identified, characterized by both a higher concentration of LDF and a higher responsiveness to antipsychotic drugs. It is suggested that since antipsychotic drugs act on dopamine receptors and LDF acts on putative serotonin receptors, dopamine and serotonin receptors may both be affected in the psychotic state. A working hypothesis is offered that links the dopamine and the serotonin hypotheses. 45 references. (Author abstract modified)

001673 Melander, A.; Danielson, K.; Vessman, J.; Wahlin, E. Dept. of Clinical Pharmacology, University of Lund, Lund, Sweden **Bioavailability of oxazepam: absence of influence of food intake.** Acta Pharmacologica et Toxicologica (Kobenhavn). 40(5):584-588, 1977.

The possible influence of food intake on the bioavailability of the anxiolytic drug oxazepam was assessed in eight healthy volunteers taking a single dose of the drug both on an empty stomach and together with a standardized breakfast meal. The serum concentrations of oxazepam were determined by gas chromatography on samples obtained before, and at numerous occasions up to 48 hours after drug administration. The results indicate that concomitant food intake has no significant influence on the bioavailability of oxazepam. 9 references. (Author abstract)

001674 Meyer, Marvin C.; Straughn, Arthur B. University of Tennessee Center for the Health Sciences, Memphis, TN 38163 **Factors affecting the bioavailability of chlorothiazide in man.** Current Therapeutic Research. 22(4):573-582, 1977.

The factors affecting the bioavailability of chlorothiazide was studied. A preliminary study of the bioavailability of 250mg and 500mg chlorothiazide tablets in three normal human volunteers indicated a urinary recovery of 7 to 38% of the administered dose. There was some increase when the same amount of the drug was administered in the form of a solution but the total recoveries still remained below 40%. When administered with a corn oil emulsion the urinary recovery was significantly increased for both tablets and solution. The results of the study indicated that chlorothiazide is apparently not well absorbed after oral administration. 13 references. (Author abstract modified)

001675 Nakra, B. R. S.; Glass, R. C.; Rees, J. A. Adult Out-Patient Services, Malcolm Bliss Mental Health Center, 1420 Grattan St., St. Louis, MO 63104 **Steady-state serum concentrations of dothiepin and northiaden after two dosage regimens of dothiepin hydrochloride (Prothiaden).** Journal of International Medical Research (Northhampton). 5(6):391-397, 1977.

A crossover study in 5 healthy volunteers which examined the serum concentrations of dothiepin and northiaden after a 25mg three times a day and a 75mg once a day regimen of dothiepin hydrochloride (Prothiaden), a tricyclic antidepressant, is evaluated. The minimum steady state level of dothiepin tended to be lower after the single daily dose, but the differences were small and not statistically significant. The approximate maximum steady state levels of dothiepin showed large intrasubject and intersubject variation and no obvious trend. The values of the desmethylated metabolite, northiaden, tended to follow the dothiepin concentrations but were lower than the parent drug. Average steady state levels tended to be very similar after both regimens with no evidence of any trend when comparing the two regimens. The study showed that the two regimens yielded similar steady state serum concentrations both of drug and metabolite but interindividual differences were large. 17 references. (Author abstract modified)

001676 Niedermeyer, E.; Yarworth, Sandy; Zobniw, Anna Maria. Johns Hopkins Hospital, 601 N. Broadway, Baltimore, MD 21205 **Absence of drug-induced beta-activity in the electroencephalogram: a sign of severe cerebral impairment.** European Neurology (Basel). 15(2):77-84, 1977.

Based on previous reports of absence of drug induced beta-activity in the EEG in epilepsy, hypoglycemic states and brain lesions, a study was made of the EEG in epileptics chronically treated with anticonvulsants known to produce fast activity. In 53 chronic epileptics with severe EEG abnormalities and under treatment with barbituric anticonvulsants, little or no fast activity was found in 44 patients. The serum concentration level (mostly phenobarbital) was in the therapeutic range in 11 patients and in the excessive range in 14 patients, while no levels were obtained in the remaining 19. Despite the lack of drug induced fast activity, fast repetitive spike discharges and

seizures with prolonged fast spike activity were demonstrated. The absence of the fast drug response is regarded as a sign of serious cerebral impairment due to the severity of the epeliptic condition. The latter could be further enhanced by toxic drug levels. 18 references. (Journal abstract modified)

001677 Nilsson, A.; Risberg, J.; Johanson, M.; Gustafson, L. Department of Psychiatry, University Hospital, Lund, Sweden **Regional changes of cerebral blood flow during haloperidol therapy in patients with paranoid symptoms.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):478-479, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, measurements of regional cerebral blood flow were used to quantitate the effects of haloperidol on activity levels in different cortical regions in treatment of 11 cases of paranoia. Regional flow was measured in 16 regions of each hemisphere by the xenon-133 inhalation technique, using the initial slope index as the main flow parameter. A standardized global rating scale was used to evaluate the clinical psychiatric picture and paranoid symptoms, and cognitive and projective tests were performed to elucidate signs of organic dementia and personality impairment. Results indicated the possible significance of activation in fronto-temporal cortical regions for abnormal mental reactions like paranoid delusions and the deactivating effect of antipsychotic drugs on these structures. 6 references.

001678 Ogura, C.; Tamai, A.; Kuda, K.; Nakamura, K.; Akamatsu, T.; Setogawa, T.; Matsuura, H. Department of Neuropsychiatry, Tottori University School of Medicine, Yonago, Japan **Relationship between physical findings and related subjective symptoms in neuropsychiatric patients with somatic complications -- with special reference to ophthalmologic observations.** Comprehensive Psychiatry. 18(4):347-355, 1977.

The relationship between physical signs and subjective symptoms was examined on ophthalmological abnormalities in 306 neuropsychiatric inpatients, mainly schizophrenics, and 89 control cases with pulmonary tuberculosis. At ophthalmological examination a variety of abnormal findings were revealed in 268 cases. As a result of clinical interview using a definite questionnaire, subjective symptoms were found in 154, being significantly lower than 69 in tuberculosis patients. Accordance between subjective symptoms and abnormal findings was found more often in cases of tuberculosis than in cases of neuropsychiatric patients. Among cases showing discordance, absence of subjective symptoms in spite of presence of abnormal findings, was observed more frequently in neuropsychiatric patients, especially in schizophrenics with highly advanced emotional disorder. Abnormal findings which were apt to be accompanied with no subjective symptoms were disorders of visual acuity, and opacities of the cornea and the lens. Existence of subjective symptoms without any abnormal findings was more remarkable in the tuberculosis patients than in the neuropsychiatric patients. In the study of the relation between absence of subjective symptoms and administered psychotropic drugs, the amount of drugs administered during the day of ophthalmological examination, the period from the beginning of therapy to the examination, the total amount of psychotropic drugs and others were calculated. Cases having no subjective symptoms in spite of presence of abnormal findings presented higher levels of drug dosage and also longer periods in the whole term than cases having subjective symptoms corresponding to abnormal findings, but there was no significant difference. 9 references. (Author abstract modified)

001679 Pandey, G. N.; Ericksen, S. E.; Ostrow, D. G.; Davis, J. M.; Baker, J.; Tosteson, D. C. Illinois State Psychiatric Institute, Chicago, IL 60612 **Lithium-sodium countertransport in human red cells and in vivo lithium distribution between red cells and plasma.** Pharmacologist. 19(2):206, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, the possibility that the interindividual variation in the steady state lithium (Li) ratio (red cell Li/plasma Li) in patients treated with Li carbonate may be caused by variations in the Li/sodium (Na) countertransport system was discussed and a study of this possibility in patients was reported. The magnitude of Li/Na countertransport in patients exhibiting a high Li ratio was very much reduced. Some of the relatives of a patient showing high in vivo Li ratio also had reduced Li/Na countertransport, suggesting that the reduction in Li/Na countertransport may be inherited. In 21 patients studied, the magnitude of countertransport was inversely correlated with the in vivo Li ratio. It is suggested that the countertransport system in patients showing high in vivo Li ratio may be defective. (Author abstract modified)

001680 Piafsky, Kenneth M.; Sitar, Daniel S.; Ogilvie, Richard I. Clinical Pharmacology Div., Montreal General Hospital, 1650 Cedar Ave., Montreal, Quebec H3G 1A4, Canada **Effect of phenobarbital on the dispostion of intravenous theophylline.** Clinical Pharmacology and Therapeutics. 22(3):336-339, 1977.

The effects of long-term use of phenobarbital on the disposition of intravenous doses of theophylline were investigated in normal male subjects before and after treatment with phenobarbital for 2 weeks. Although there was some variation in disposition of the two drugs, there were no significant effects of phenobaribtal on theophylline kinetics. It is concluded that theophylline dosage need not be altered during concomitant administration of phenobarbital. 15 references. (Journal abstract modified)

001681 Pickard, J. D.; Rose, J. E.; Cooke, M. B. D.; Blair, I. McL.; Strathdee, A. MRC Cerebral Circulation Research Group, Institute of Neurological Sciences, Glasgow, Scotland **The effect of salicylate on cerebral blood flow in man.** Acta Neurologica Scandinavica (Kobenhavn). 56(Supplementum 64):422-423, 1977.

In a paper presented at the proceedings of the Symposium on Cerebral Function Metabolism and Circulation, Copenhagen, Denmark, 1977, the effect of salicylate on cerebral blood flow (CBF) in man in terms of blocking the effect of carbon dioxide on cerebral circulation while maintaining autoregulation and the implications for use of salicylates in transient ischemic attacks was studied. The labeled xenon inhalation technique was used to measure CBF in male volunteers (23 years old to 34 years old) with no recent medication, during air breathing and during hypercapnic condition. The blood flow response to hypercapnia with and without aspirin was determined. Salicylates at the higher dose appeared to block the response of CBF to carbon dioxide. It is recommended that when salicylates are used in transient ischemic attacks, the dose should be the minimum required to inhibit platelet aggregation if the capacity of vessels distal to stenotic lesions to dilate with hypercapnia is not to be restricted. 4 references.

001682 Piraino, Anthony J.; Di Gregorio, G. John. Hahnemann Medical College, Philadelphia, PA 19102 **Comparative availability of diazepam (D) in human plasma (P), parotid saliva**

(PS) and mixed saliva (MS) and its relationship to plasma protein binding. Pharmacologist. 19(2):128, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the comparative availability of diazepam in human plasma, parotid saliva, and mixed saliva following a single oral dose of the drug, and of the relationship between availability and plasma protein binding, was reported. The in vitro serum binding of diazepam was also investigated, and the data were found to agree closely with those of serum samples collected following oral administration of diazepam. Equilibrium dialysis studies confirmed that diazepam did not bind with either parotid saliva or mixed saliva. Comparative availability studies revealed a parallel relationship between the concentrations of diazepam in simultaneously collected plasma and parotid saliva. However, no relationship was found between the concentrations of drug in plasma and mixed saliva. The results of equilibrium dialysis protein binding studies confirmed that the concentration of diazepam in parotid saliva compares favorably with that found to be free from protein binding and therefore pharmacologically active. (Author abstract modified)

001683 Post, Robert M.; Cramer, Hinrich; Goodwin, Frederick K. Section on Psychobiology, Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Cyclic AMP in cerebrospinal fluid of manic and depressive patients.** Psychological Medicine (London). 7(4):599-605, 1977.

Cyclic 3',5'-adenosine monophosphate (cAMP) was measured in cerebrospinal fluid (CSF) of manic and depressive patients with and without probenecid administration both before and during treatment with various psychotropic drugs. Oral probenecid (100mg/kg) produced substantial cAMP accumulations in CSF suggesting a probenecid sensitive transport mechanism for cAMP. Baseline and probenecid induced accumulations of cAMP were not significantly different in manic and depressed patients, while baseline levels in depressed patients were higher than those in neurological controls. Imipramine, amitriptyline, lithium, tryptophan, and electroconvulsant therapies did not significantly alter levels or accumulations of cAMP in CSF of depressed patients. 47 references. (Author abstract)

001684 Preziosi, P.; Nistico, G. Institute of Pharmacology, IInd Faculty of Medicine, University of Naples, Via S. Papysini 5, I-80131 Naples, Italy **Psychotropic drugs: mechanism of action at the neurotransmitter level.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 15(11):497-518, 1977.

Although the intimate mechanism by which psychotropic agents exert their therapeutic effects is still not completely clear, a large bulk of evidence is reviewed supporting the existence of a close correlation between their clinical antipsychotic activity and the ability to affect by different mechanisms brain monoamines and/or other real or putative neurotransmitters. Neuroleptic drugs of the phenothiazine type and related classes possess a blocking effect on dopaminergic transmission in nigrostriatal, mesolimbic and mesocortical areas; experiments supporting both a presynaptic and postsynaptic site of action are described, together with the interference at the molecular level with DA sensitive adenylate cyclase activity. Anxiolytics seem to produce their therapeutic effects through a decrease in catecholaminergic and serotoninergic turnover although new avenues have been opened by some recent reports indicating a facilitation of GABAergic and glycinergic transmission in CNS. The mechanisms by which antidepressant drugs enhance monoaminergic tonus are reviewed as well as the sites and possible modes of action of d-amphetamine which allow explanation of behavioral, therapeutic and toxic effects of this powerful psychostimulant drug. 265 references. (Author abstract modified)

001685 Rinne, Urpo K.; Marttila, Reijo; Sonninen, Vesa. Department of Neurology, University of Turku, SF-20520 Turku 52, Finland **Brain dopamine turnover and the relief of Parkinsonism.** Archives of Neurology. 34(10):626-629, 1977.

The relationship between dopamine receptor activation and the relief of parkinsonian clinical features was studied in 40 patients with Parkinson's disease. Treatment with dopamine receptor agonists, piribedil or bromocriptine, decreased significantly both the basal level and probenecid induced accumulations of homovanillic acid (HVA) in the CSF. But there were not changes in the concentrations of 5-hydroxyindole acetic acid (5-HIAA). Correlation analyses showed that patients who improved with both the dopamine agonists used had significantly lower probenecid response of HVA in the CSF and a less severe disease condition than those without beneficial effect. This relationship between dopamine receptor activation and improvement of parkinsonian disability suggests that the therapeutic efficacy of dopamine receptor agonists depends on the functional capacity of brain dopaminergic mechanisms. 35 references. (Author abstract)

001686 Rowe, H. M.; Lemberger, L.; Carmichael, R. H.; Bymaster, F. P.; Horng, J. S.; Wong, D. T. Lilly Research Laboratories, Clinical Research Division, Indianapolis, IN 46202 **Fluoxetine, a serotonin uptake inhibitor, in normal human subjects.** Pharmacologist. 19(2):166, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects in humans of fluoxetine hydrochloride, which has been shown to inhibit serotonin (5-HT) uptake by rat brain synaptosomes at doses that do not affect norepinephrine (NE) or dopamine uptake, was reported. Unlike nisoxetine and imipramine, fluoxetine produced no change in sensitivity to tyramine and NE infusions when compared to a period of placebo administration. Platelets collected from these subjects showed a 42% inhibition on day 4 and a 65% inhibition on day 7 of their ability to concentrate 5-HT. No perceptible changes in behavior or adverse effects were noted. Plasma levels of fluoxetine approached steady state; however, norfluoxetine, an active metabolite, continued to increase throughout the 7 days. (Author abstract modified)

001687 Rowe, J. W.; Costa, P. T., Jr.; Burney, S.; Podolsky, S. Normative Aging Study, V.A. Outpatients Clinic, Boston, MA 02108 **Impact of age on anterior pituitary hormones in adult males.** Gerontologist. 17(5, Part I):112, 1977.

In a paper read at the 30th meeting of the Gerontological Society, San Francisco, November 1977, basal and L-dopa stimulated plasma levels of LH, FSH, TSH, HGH, and prolactin were measured by radioimmunoassay in 36 healthy young (mean age 35) and 43 healthy old (mean age 65) males to determine the impact of age on anterior pituitary hormones in adult males. There were no age differences in basal levels of HGH, LH, TSH, or prolactin. Basal gonadotropin level of FSH was significantly higher in old males. The stimulated levels, drawn 1 hr after 500mg L-dopa, showed a significant increase in FSH and LH in old Ss but no effect of L-dopa on gonadotropins in young Ss. L-dopa induced increases in HGH and decreases in

TSH and prolactin which were of similar magnitude in both age groups. (Journal abstract modified)

001688 Saxena, R. C.; Thacore, V. R.; Suri, M. L.; Agarwal, T. N.; Bhargava, K. P. Upgraded Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow, India **Electroencephalographic studies with i.v. methaqualone in man.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 43(6):876-879, 1977.

To examine the central effects of methaqualone by electroencephalography (EEG) in man, methaqualone was administered intraveneously to 17 physically healthy males suffering from minor psychiatric ailments. Discrepancies between clinical and EEG signs were thus seen. EEG patterns resembled those after barbiturates and the effect is dose dependent. Differences between methaqualone and barbiturates are discussed. The EEG patterns are potentiated by thioridazine and antagonized by imipramine. 24 references. (Author abstract modified)

001689 Shader, Richard I.; Greenblatt, David J.; Harmatz, Jerold S.; Franke, Kate; Koch-Weser, Jan. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Absorption and disposition of chlordiazepoxide in young and elderly male volunteers.** Journal of Clinical Pharmacology. 17(11 & 12):709-718, 1977.

The pharmacokinetics of oral chlordiazepoxide were studied in 28 young and eight elderly male volunteers, in good health. Subjects received 25mg chlordiazepoxide (CDX) hydrochloride with water in the fasting state. Multiple venous blood samples drawn during 24 hours after the dose were assayed for concentrations of CDX and its major pharmacologically active metabolite desmethylchlordiazepoxide (DMCDX). Peak CDX blood levels in the elderly subjects were lower and were reached later after the dose than in the young volunteers, suggesting a slower rate of absorption in the elderly. The mean elimination halflife of CDX in the elderly was significantly longer than in the young subjects and CDX clearance in the elderly was significantly less than in the young. Appearance in the blood of DMCDX was also significantly reduced in the elderly. The findings were not influenced by smoking habits or by concurrent use of other drugs. Because of its decreased clearance in elderly individuals, accumulation of CDX during chronic therapy may be greater in elderly than in young patients. The clinical significance of this is not established, since generation of the pharmacologically active metabolite DMCDX is also reduced. 29 references. (Author abstract)

001690 Stefanis, C. N.; Lykouras, E.; Garelis, E.; Varsou, E. Athens University, Dept. of Psychiatry, Athens, Greece **Cyclic AMP in the plasma of chronic schizophrenics, before and after treatment.** Progress in Neuro-Psychopharmacology. 1(3/4):323-327, 1977.

To determine pretreatment and posttreatment plasma levels of cyclic adenosine monophosphate (cyclic AMP) in chronic schizophrenics as a means of gaining information on the effects and action of pimozide, a model dopamine receptor blocker in this nucleotide, concentrations of cAMP in plasma were measured by a protein binding method in a selected group of 10 chronic schizophrenics before and after pimozide treatment. Subjects were hospitalized for a mean period of 23.7years and had not received any physical treatment for 1 to 10 years. Ten age matched volunteers from the hospital staff served as controls. Before treatment, cAMP in the patient group was not significantly different from control values. After pimozide (8mg/day for one month) there was a striking decrease of cAMP by far exceeding normal levels. Clinical improvement was slight and extrapyramidal manifestions were moderate in most patients. The overshooting effect of pimozide on cAMP is taken to provide evidence of inadequate mechanisms of compensation in schizophrenia. 20 references. (Author abstract modified)

001691 Swulman, Ralph; Diewold, Patricia. Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada A **two-dose dexamethasone suppression test in patients with psychiatric illness.** Canadian Psychiatric Association Journal (Ottawa). 22(8):417-422, 1977.

To examine the discriminative validity of the dexamethasone suppression test in the diagnosis of endogenous depression and to evaluate the effects of the drug on adrenocortical overactivity, 34 consecutively admitted acute psychiatric patients diagnosed as manic, primary depressive, or schizophrenic were administered dexamethasone six times daily for a period of 48 hours on 4 consecutive days. Dose for the first administration period was 2mg, and 6mg for the second period. Analysis of data indicates that 11 of 34 acute psychiatric inpatients demonstrated abnormal dexamethasone suppression characterized by morning and/or midafternoon escape from suppression. This abnormality of suppression was found in primary depression, in mania, and in acute schizophrenia. In primary depression, the presence of abnormal dexamethasone suppression failed to discriminate endogenous depressed from other depressed subjects. Because nonsuppression to a high dose of dexamethasone is also found in patients with ectopic adrenocorticotrophic hormone secretion and in patients with autonomous adrenal tumors, caution is necessary in the interpretation of nonsuppression which persists after recovery from psychiatric illness. As patients with Cushing's syndrome of uncertain etiology may be referred to a psychiatrist for a diagnostic evaluation, the psychological correlates of abnormal dexamethasone suppression need to be established with greater certainty. 23 references. (Author abstract modified)

001692 Terenius, Lars; Wahlstrom, Agneta; Agren, Hans. Dept of Medical Pharmacology, University of Uppsala, Box 573, S-751 23 Uppala, Sweden **Naloxone (Narcan) treatment in depression: clinical observations and effects on CSF endorphins and monoamine metabolites.** Psychopharmacology (Berlin). 54(1):31-33, 1977.

To study the effect of naloxone on mood states and several metabolite levels in depressed subjects, naloxone was given to five depressed patients in six trials for a duration of 6 to 12 days. The cerebrospinal fluid endorphin and monoamine metabolite content was analyzed before and after naloxone treatment. No positive effect on mood level was observed. However, an abrupt worsening of symptoms was noted in two cases on discontinuation of treatment. Decreasing values of endorphin Fraction I as a result of treatment was noted as a general trend. Fraction II, although elevated, showed no distinct trend. The results suggest that naloxone treatment changes endorphin and serotonin activity, though not to a clinically observable extent. 9 references. (Author abstract modified)

001693 Trush, M. A.; Wilson, M. E.; Van Dyke, K. Department of Pharmacology, West Virginia University Medical Center, Morgantown, WV 26506 **Generation of electronic excited states (EES) by tricyclic antidepressants: molecular aspects.** Pharmacologist. 19(2):163, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in

Columbus, Ohio, August 1977, a series of studies performed to determine if the production of electronic excited states (EES) as indicated by a chemiluminescence (CL) response as has been previously reported with imipramine always results when a tricyclic antidepressant is added in vitro to human polymorphonucleotides (PMNs) was reported. CL was elicited by desipramine and iprindole, but not by amitriptyline, nortriptyline, protriptyline, or doxepin. Amitriptyline, nortriptyline, protriptyline and doxepin inhibited the amount of CL induced by zymosan, a response which was potentiated by imipramine, desipramine, and iprindole. The response to imipramine was inhibited by superoxide dismutase but not by agents which modify cellular activity and decrease phagocytosis induced CL. Addition of imipramine to the xanthine oxidase/purine superoxide generating system also produced CL. It is suggested that generation of EES by tricyclic antidepressants may be defined by a certain molecular structure (nitrogen at the 5 position) and that the CL observed upon addition of imipramine to PMNs may result in part from the activation of imipramine by purine superoxide. (Author abstract modified)

001694 Wode-Helgodt, B.; Eneroth, P.; Fyro, B.; Gullberg, B.; Sedvall, G. Department of Psychiatry, St. Goran's Hospital, S-112-81 Stockholm, Sweden **Effect of chlorpromazine treatment on prolactin levels in cerebrospinal fluid and plasma of psychotic patients.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(4):280-293, 1977.

In schizophrenic patients, levels of prolactin in cerebrospinal fluid (CSF) and plasma were determined by radioimmunoassay before and after 2 and 4 weeks of treatment with chlorpromazine (CPZ). Before treatment, low levels of immunoreactive prolactin like material (PRL) were found in the CSF of most patients. The concentration in CSF was about 20% of the plasma level. In CSF but not in plasma, the pretreatment level of PRL was significantly higher in women than in men. During CPZ treatment, the PRL levels in CSF as well as in plasma were significantly elevated in both sexes after 2 as well as 4 weeks. The elevation was significantly greater in women, and was similar at the two time intervals studied. There was a significantly positive relationship between the dose of CPZ and the PRL elevation in both body fluids in both men and women. During treatment, there was a significant correlation between the change in PRL levels in CSF and plasma in both men and women. 33 references. (Author abstract modified)

001695 Yesavage, Jerome A.; Tinklenberg, Jared R.; Berger, Philip A.; Hollister, Leo E. Dept. of Psychiatry, Stanford University, Stanford, CA 94305 **Drug improving cerebral metabolism in dementia.** Gerontologist. 17(5, Part I):135, 1977.

In a paper read at the 30th meeting of the Gerontological Society, San Francisco, November 1977, several drugs were tested which have been claimed to improve cerebral intermediary metabolism in the aged, a defect in which may play a role in mental deterioration in old age. Over 100 outcome studies are critically reviewed. It is concluded that while further research is needed with these drugs, they do have a mild effect in senile dementia and that significantly more studies claim positive results for drugs with primary metabolic action than do studies using drugs with solely vasodilator effects. (Journal abstract modified)

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001696 Ban, Thomas A. Vanderbilt University, Nashville, TN **Perspectives in biological psychiatry. part 3: schizophrenia and organic brain syndrome.** Psychosomatics. 18(4):35-38, 44-45, 1977.

Schizophrenia and chronic organic brain syndrome are discussed within the context of a qualitative and quantitative analysis of the behavioral changes affected by psychopharmacological agents. The dopamine hypothesis of schizophrenia is reviewed along with other neurotransmitters such as acetylcholine. Piracetam is discussed in terms of its possible significance in organic brain syndrome, and psychopharmacological aspects of aggression are reported. It is suggested that a new era of understanding is at hand in which learned and inherited patterns of behavior will not be separated and in which the biochemical and genetic basis of conditioning will be revealed. 87 references.

001697 Barkley, Russell A. Bowling Green State University, Bowling Green, OH **The prediction of differential responsiveness of hyperkinetic children to methylphenidate. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-23186 HC$15.00 MF$8.50 174 p.

The effects of methylphenidate on activity level and attention of hyperactive children were studied, with emphasis on variables predicting the degree to which Ss improved. Ss were 36 diagnosed hyperkinetic and normal boys ages 5 to 12, observed on three occasions: 1) all Ss off drugs; 2) hyperkinetic Ss on drug or placebo; 3) crossover of drug and placebo Ss compared to phase 2. At each observation, Ss were evaluated on activity level and attention; parental ratings and math and reading tests were also used. Methylphenidate significantly improved activity levels in various activities in hyperactive Ss. Attention span and concentration on tasks were also improved. Pretreatment levels of inability to concentrate on structured tasks were the best predictors of global improvement during drug treatment. Hyperactive Ss were significantly more active, had shorter attention spans, were less able to concentrate on tasks, were less able to inhibit locomotor activity, and were viewed by their parents as more active than normal children. They were observed to increase their task irrelevant activity over time. Despite positive drug effects, it is noted that clinical observations suggest that methylphenidate may reduce the hyperactive child's responsiveness to his environment. (Journal abstract modified)

001698 Barkley, Russell A. Department of Neurology, Medical College of Wisconsin, Milwaukee Children's Hospital, 1700 West Wisconsin Avenue, Milwaukee, WI 53233 **The effects of methylphenidate on various types of activity level and attention in hyperkinetic children.** Journal of Abnormal Child Psychology. 5(4):351-369, 1977.

The effects of methylphenidate on a number of objective measures of activity level and attention in hyperkinetic children were assessed on three repeated occasions in four types of settings: free play, movie viewing, testing, and restricted play periods. Subjects were 36 boys between 5 and 12 years of age and of average intelligence. Of these, 18 were diagnosed as hyperkinetic and participated in a double-blind drug/placebo crossover design. The remaining 18 boys, matched in age and IQ with the hyperkinetic children, served as a control group and received no drugs. Results indicate that compared to placebo, methylphenidate significantly reduces wrist, ankle, locomotor, and seat movement activity in the hyperkinetic children, regardless of the type of setting in which the measures are taken. Relatively fewer significant drug effects were noted on the measures of concentration or attention. While concentration to reaction time, maze performance, and a movie viewing task inproves during drug treatment, the length

of attention to toys in free play was not significantly improved. Parental ratings of activity level are also improved by the drug. The hyperkinetic children are also observed to increase their level of task irrelevant activity over time while control children remained relatively stable in activity over repeated assessment. Despite the positive drug effects, clinical observations suggested that methylphenidate may have reduced the interest of some children in their environment. 26 references. (Author abstract)

001699 Bert, J.; Saier, J.; Dufour, H.; Scotto, J. C.; Julien, R.; Sutter, J. M. Service de Neurophysiologie Clinique, Centre Hospitalo-Universitaire de la Timone, F-13385 Marseille Cedex 4, France **/Modification of sleep induced in acute and chronic administration of lithium./** Modifications du sommeil provoquees par le lithium en administration aigue et en administration chronique. Electroencephalography and Clinical Neurophysiology (Amsterdam). 43(5):745-748, 1977.

The sleep of two groups of subjects receiving acute and chronic administration of lithium was studied. Ten normal controls after 17 days of lithium had a significant decrease of paradoxical sleep duration, with an increase of paradoxical sleep (PS) latency. A second group of ten manic-depressive patients who had received lithium for about 22 1/2 months when they were recorded showed a greater amount of slow-wave sleep than the control group before lithium, but the different of PS duration was only related to a first night effect. It is suggested that sleep changes induced by lithium are different according to the duration of lithium administration, and are less important than those induced by most of the antidepressants. 10 references.

001700 Betts, T. A.; Blake, Alison. Department of Psychiatry, University of Birmingham, Queen Elizabeth Hospital, Birmingham B15 2TH, England **The psychotropic effects of atenolol in normal subjects: preliminary findings.** Postgraduate Medical Journal (Oxford). 53(3):151-156, 1977.

A paper presented at a symposium on atenolol held in Nice, France October 4-6, 1976 discusses a comparative study of the effects of atenolol, chlordiazepoxide and placebo on the subjective feelings of normal young women which showed that atenolol significantly induced feelings of relaxation and well-being in these subjects as did chlordiazepoxide. Unlike chlordiazepoxide, however, atenolol had no sedative effect. Objective assessment of the subjects confirmed these findings. It is suggested that atenolol may be particularly suitable for the symptomfree hypertensive patient and that further studies should be undertaken into whether it has a central action in the nervous system and into its effects on clinically anxious patients. 11 references. (Author abstract)

001701 Biersner, Robert J.; Hall, David A.; Neuman, Tom S.; Linaweaver, Paul G. Naval Submarine Medical Research Laboratory, Box 900, Naval Submarine Base, Groton, CT 06340 **Learning rate equivalency of two narcotic gases.** Journal of Applied Psychology. 62(6):747-750, 1977.

Two groups of U.S. Navy divers were tested for (a) digit span forward and backward and (b) simple and difficult paired-associate learning while breathing normal air or a narcotic gas (nitrous oxide or hyperbaric nitrogen). The first group of 21 divers breathed 30% nitrous oxide (N2O) and the second group of 11 divers breathed hyperbaris nitrogen (Hyper N2) at a simulated ocean depth of 65 m. The two forms of the digit span and paired-associate measures were from the Wechsler Memory Scale, and were administered in a counterbalanced fashion between normal and narcotic conditions. Results showed that forward and backward digit span remained normal during N2O and Hyper N2 narcosis, whereas simple and difficult paired-associate learning was impaired uniformly and significantly by both of the narcotic gases. These results indicate that the long-term memory effects of these two narcotic gases are similar and that the narcotic properties of both gases may be equivalent. 12 references. (Author abstract)

001702 Cocchi, R. Ospedale Neuropsichiatrico della Provincia di Cuneo in Racconigi, Settori di Alba-Bra e Mondovi, Cuneo in Racconigi, Italy **/Hypothesized adrenergic/noradrenergic substitution in habitual infantile masturbation: two cases./** L'ipotesi di sostituzione adrenergica-noradrenergica nella masturbazione infantile abituale -- 2 casi. Rassegna di Studi Psichiatrici (Siena). 66(1):9-16, 1977.

A test was made of the hypothesis that habitual masturbation is a defense mechanism for avoiding depression, and that by temporary adrenergic substitution of a noradrenergic component, Norden, such behavior can be diminished. Clinical cases of two males, ages 6 and 11, to whom Norden was given, demonstrated that masturbation did in fact greatly diminish. It is concluded, however, that not enough evidence exists as yet to demonstrate the uncontested validity of this hypothesis. 23 references.

001703 Counts, Willie Roger. Arizona State University **The effects of Darvon-N on retention of specific learning tasks during heroin detoxification. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-26905 HC$15.00 MF$8.50 118 p.

The effects of Darvon-N during heroin detoxification were studied to determine whether the drug produces state dependent learning and, if so, whether the learning can be identified by specific learning tasks. Ss were equally distributed into three groups: 1) Darvon-N to Darvon-N (D-D); 2) Darvon-N to placebo (D-ND); and 3) drug free to drug free (ND-ND). Three null hypotheses, corresponding to the three learning tasks (word recall, picture arrangement and recall, and four way picture choice) could not be rejected. A qualitative comparison of mean posttest scores shows that the mean scores on the three tasks for the ND-ND group were greater than those for the D-D and D-ND groups. Mean scores of the word recall and picture arrangement and recall tasks for the D-D groups were greater than those for the D-ND. It is concluded that Darvon-N probably does not show state dependent learning effects when used for heroin detoxification, especially for the tasks studied. It is suggested that Darvon-N could be used in detoxification, especially since it reduces the physical impairments of methadone. (Journal abstract modified)

001704 D'Elia, G.; Lehmann, J.; Raotma, H. no address **Evaluation of the combination of tryptophan and ECT in the treatment of depression: 1. clinical analysis.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(4):303-318, 1977.

A double-blind evaluation of the antidepressant efficacy of treatment with a combination of orally administered L-tryptophan (L-TP) and electroconvulsive therapy (ECT) was made in patients suffering from endogenous depression. The patients were randomly assigned to two groups, one treated with L-TP (6g daily) and unilateral ECT, the other two groups in several measures ECT. There was a good agreement between the two groups in several measures of antidepressant efficacy: doctors' and patients' ratings of depressive symptoms, and doctors' global rating of therapeutic effect 4 days and 1 month after the last ECT. In the L-TP group, however, there was significantly

better effect on retardation symptoms in the nurses' rating scale. This difference, which is not consistent with other measures of amelioration, contributes at most, to a marginal therapeutic addition to the antidepressant effect of ECT. It is concluded that oral administration of L-TP, in the dose of 6g daily, is not of practical value for potentiating the antidepressant efficacy of ECT. 104 references. (Author abstract modified)

001705 Davis, Jonathan L.; Lewis, Stephen B.; Gerich, John E.; Kaplan, Roy A.; Schultz, Thomas A.; Wallin, John D. Clinical Investigation Center, Naval Regional Medical Center, Oakland, CA 94627 **Peripheral diabetic neuropathy treated with amitriptyline and fluphenazine.** Journal of the American Medical Association. 238(21):2291-2292, 1977.

The treatment of peripheral neuropathy associated with diabetes with amitriptyline and fluphenazine, which resulted in remarkable relief of pain in one patient, and was subsequently tried in seven other cases, is reported. The improvement was marked in all cases, and manifested by increased ability to sleep without interruption due to pain, increased ease in performing usual activities, and discontinuation of analgesic use. These improvements in well-being occurred within 48 hours with fluphenazine and 5 days with amitriptyline, unaccompanied by changes in nerve conduction velocity or control of hyperglycemia. Preliminary observations suggest that fluphenazine, amitriptyline, or a combination of these drugs may be useful in the management of the painful peripheral neuropathy of diabetes. 10 references.

001706 Dodrill, Carl B.; Troupin, Allan S. Epilepsy Center, Harborview Medical Center, 325 9th Ave., University of Washington, Seattle, WA 98104 **Psychotropic effects of carbamazepine in epilepsy: a double-blind comparison with phenytoin.** Neurology. 27(11):1023-1028, 1977.

The psychotropic effects of carbamazepine were evaluated with phenytoin (Dilantin) as reference agent in a counterbalanced, crossover study. Forty adult epileptics were given a series of neuropsychologic tests and the MMPI after 4 months on each agent. Most abilities were much the same with either anticonvulsant, but there were fewer errors with carbamazepine on mental tasks requiring attention and problem-solving, and some improvement in emotional status was suggested. The findings were consistent with patient reports of improvement in alertness and mental functioning. It is concluded that the results combine with the excellent anticonvulsant properties of carbamazepine to support its use as an anticonvulsant. 22 references. (Author abstract)

001707 Dowrick, Peter W.; Raeburn, John M. Department of Psychiatry, University Medical School, P. B., Auckland 1, New Zealand **Video editing and medication to produce a therapeutic self model.** Journal of Consulting and Clinical Psychology. 45(6):1156-1158, 1977.

An edited videotape to be used in a self-modeling procedure to modify the playing behavior of a 4-year-old retarded, hyperactive boy was created both while the boy was under treatment with haloperidol and while he was on no medication. Earlier, the boy had been unable to role-play suitable behaviors. With the use of psychotropic medication and video editing, a videotape was produced which when viewed by the subject had therapeutic effects. 2 references. (Author abstract modified)

001708 Feinberg, Irwin; Fein, George; Walker, James M.; Price, Leonard J.; Floyd, Thomas C.; March, Jonathan D. Veterans Administration Hospital, San Francisco, CA 94121 **Flurazepam effects on slow-wave sleep: stage 4 suppressed but number of delta waves constant.** Science. 198(4319):847-848, 1977.

To study the effects of flurazepam on slow-wave sleep, four students received 15mg flurazepam on the first drug night and 30mg for the next 7 nights. It was found that repeated administration of flurazepam reduced stage 4 sleep (high delta-wave concentration) but produced a greater increase in stage 2 duration so that total sleep time was increased. Computer analysis revealed that the increased amount of stage 2 (low delta-wave concentration) sleep provided a number and duration of delta-waves sufficient to offset the loss of delta activity in stage 4. However, the amplitude of the average delta-wave was reduced. These results demonstrate the value of direct quantification of delta-wave activity, the variable that underlies visual classification of slow-wave sleep into stages 2 to 4. They also give rise to new hypotheses regarding the relative absence of side-effects in spite of profound stage 4 suppression by flurazepam and the mechanisms by which total sleep time is increased by this drug. 21 refernces. (Journal abstract)

001709 Friedman, Judith Anne. Catholic University of America **A developmental study of selective attention in hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-19969 HC$15.00 MF$8.50 81 p.

Selective attention in hyperactive children was studied, hypothesizing that such attention is influenced by age and amphetamines and that meaningfulness differentially influences attention in normals, hyperactives, and hyperactives on drugs. Data were obtained from 72 boys in the age groups of 6 to 7 and 8 to 9 years. The selective attention task measured central and incidental recall. Results indicated that selective attention of hyperactive children is influenced by age, medication, and information load. Analysis of correlation between central and incidental recall indicated no consistent relationship as a function of age. The developmental aspects of responsiveness to medication require further investigation, along with the effect of information load on other aspects of intellectual performance. (Journal abstract modified)

001710 Fruensgaard, K.; Korsgaard, S.; Jorgensen, H.; Jensen, K. Department of Psychiatry, Odense University Hospital, DK-5000 Odense, Denmark **Loxapine versus haloperidol parenterally in acute psychosis with agitation: a double-blind study.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(4):256-264, 1977.

A comparison of loxapine and haloperidol parenterally in acute psychotic, agitated patients was carried out as a randomized double-blind trial. The trial covered 15 patients in each group, and the diagnoses were psychogenic psychosis (18 cases) and acute schizophrenia (12 cases). Sedation, agitation/excitement and aggressive behavior were scored prior to treatment and at specified time intervals after the first two injections. A significantly stronger and more rapid sedation effect was seen in the loxapine group when compared with haloperidol group. Furthermore, there was a tendency to a better control of agitation/excitement and aggression in the loxapine group. In spite of prophylactic treatment with biperiden, seven of 15 patients in the haloperidol group experienced extrapyramidal side-effects. The most frequent side-effect in the loxapine group was atypical dizziness. Loxapine i.m. appears to be a valuable drug in cases of acute psychosis where strong sedation as well as strong antipsychotic effect are necessary for behavioral control. 6 references. (Author abstract modified)

001711 Gibson, H. B. Hatfield Polytechnic, Hatfield, England **Animal hypnosis and human hypnosis: new experimental evidence relating to an old controversy.** Psychologia (Kyoto). 20(3):136-144, 1977.

The current position relating to animal hyposis in relation to human hypnosis is briefly reviewed and it is suggested that progress in animal studies may reactivate the old controversy as to whether there is any useful analogy. The present results arose from another study in which 88 Ss were tested for hypnotic susceptibility and then divided into a placebo group receiving nicotinic acid, and a drug group receiving diazepam plus nicotinic acid, and retested. While both placebo and drug groups of males (n=32) increased slightly on retest, with the females (n=39) the placebo group decreased slightly and the drug group decreased significantly on retest. It is suggested that these results can be compared with the animal studies using tranquilizing drugs and habituation as the results are similar, and support the fear hypothesis. It is suggested that in the conditions of the experiment, a greater proportion of the females may have been situationally more fear prone. 34 references. (Author abstract)

001712 Gillin, J. Christian; van Kammen, Daniel P.; Post, Robert; Bunney, William E., Jr. Unit on Sleep Studies, APB, NIMH, Building 10, Room 3N224, Bethesda, MD 20014 **Effects of prolonged administration of pimozide on sleep-EEG patterns in psychiatric patients.** Communicating in Psychopharmacology. 1(3):225-232, 1977.

To determine effects of prolonged pimozide administration on EEG sleep patterns in psychiatric patients, EEG sleep patterns and nurses' ratings of behavior were studied before, during, and after a clinical trial of pimozide in ten psychiatric inpatients with various diagnoses. Total sleep time, sleep efficiency, and stage II (both minutes per night as a percentage of total sleep time) were significantly increased during treatment with pimozide as compared with baseline before treatment and withdrawal afterwards. Sleep changes do not correlate significantly with clinical changes rated by nurses. Implications for the role of dopamine in maintaining wakefulness are discussed. 9 references. (Journal abstract modified)

001713 Goetzl, Ugo; Grunberg, Frederic; Berkowitz, Bernard. Inpatient Unit, Albany Medical College, Albany, NY **Lithium carbonate in the management of hyperactive aggressive behavior of the mentally retarded.** Comprehensive Psychiatry. 18(6):599-606, 1977.

Three case studies are presented which illustrate the use of lithium carbonate in the management of hyperactive aggressive behavior in mentally retarded young adults. All three cases responded well to lithium carbonate. Two possible explanations for this therapeutic response to lithium are discussed. First, mentally retarded can be afflicted with manic-depressive illness and can respond to lithium carbonate as any other manic-depressive who is not mentally retarded. Secondly, lithium carbonate has a specific antiaggressive effect independent of the presence of a manic-depressive illness. It is noted that in all three patients, lithium carbonate was found more effective in controlling their aggressive behavior than the neuroleptics used for behavior control. 13 references.

001714 Griffith, J. D.; Jasinski, D. R.; Pevnick, J. National Institute on Drug Abuse Addiction Research Center, P.O. Box 12390, Lexington, KY 40511 **Effect of alpha-methyltyrosine (MT) pretreatment on d-amphetamine (A) and morphine (M) induced mood in man.** Pharmacologist. 19(2):230, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a study of the effects of alpha-methyltyrosine (MT) pretreatment on the subjective effects of amphetamine or morphine in nontolerant addicts was reported. Amphetamine, morphine, or placebo were administered subcutaneously after pretreatment with oral MT or placebo. Although MT attenuated the pressor effects of amphetamine, it had little influence on amphetamine induced or morphine induced euphoria. Subjects had no difficulty in distinguishing either drug from placebo despite MT pretreatment. MT tended to modify some of the unpleasant effects of amphetamine, such as insomnia, nervousness, and anorexia. MT itself produced some sedation and dysphoria; these effects could be reversed by amphetamine. It is concluded that MT does not block the euphoriginic effects of acute, moderate doses of amphetamine or morphine in nontolerant humans. 1 reference. (Author abstract modified)

001715 Griffiths, Roland R.; Stitzer, Maxine; Corker, Kevin; Bigelow, George; Liebson, Ira. Dept. of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Drug-produced changes in human social behavior: facilitation by d-amphetamine.** Pharmacology Biochemistry and Behavior. 7(4):365-372, 1977.

The effects of oral d-amphetamine on human social and verbal behavior were studied using repeated observations within subjects under double-blind conditions. In the first experiment socializing and standing were measured during daily 6 hour sessions using a time sampling observation procedure in a residential research ward. d-Amphetamine increased socializing in all three subjects studied, but only increased standing in one of the subjects. In the second experiment throat microphones and voice operated relays were used to measure automatically quantitative aspects of dyadic verbal interactions during 1 hour daily sessions. Total speaking time showed dose related increases in five of the seven subjects receiving d-amphetamine. Adjective checklist self-report scores indicating stimulant drug effects were as sensitive and reliable as the speaking measure to the effects of d-amphetamine in these subjects. Speaking time also increased in two of the eight partners who received placebo when the subjects with whom they were paired received d-amphetamine, a socially mediated indirect drug effect. Adjective checklist scores of the partners receiving placebo were not changed when the paired subjects received d-amphetamine. It is concluded that under controlled experimental conditions, the naturalistic human behaviors of socializing and speaking are sensitive dependent variables for behavioral pharmacology research. 27 references. (Author abstract modified)

001716 Gupta, B. S. Department of Psychology, Guru Nanak Dev University, Amritsar, India **Dextroamphetamine and measures of intelligence.** Intelligence. 1(3):274-280, 1977.

The effects of dextroamphetamine, a central stimulant, on the test scores of fluid and crystallized intelligence for a sample of 320 male highschool students varying on the neuroticism and extraversion dimensions of personality was investigated. An analysis of performance scores revealed that drug treatments were significant variables for the fluid intelligence test and were dependent on the different personality groups influencing their arousal or drive level. The only variable that significantly affected the crystallized composite raw scores was the linear trend of treatment and the insignificant interaction of personality and treatments indicated that individuals did not differ in their susceptibility to drug effects on the

crystallized test. It is concluded that these results support the hypothesis that the drug will have a differential effect on the test scores of fluid and crystallized intelligence. 21 references.

001717 Horner, Gary Caroll. University of Missouri, Kansas City, MO **Hyperactive and non-hyperactive children's self-determined levels of stimulation. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-27335 HC$15.00 MF$8.50 88 p.

Differences in the self-determined preferred levels of stimulation of learning disabled hyperactive and nonhyperactive children were investigated, along with the effect of methylphenidate (Ritalin) on hyperactive Ss self-determined levels. It was predicted that: 1) elementary school hyperactive children would have higher self-determined preferred levels than nonhyperactives for visual, auditory, and somatosensory modalities; and 2) Ritalin would significantly lower these levels for the hyperactive Ss. Neither hypothesis was supported for the experimental conditions. Results suggested that amount of environmental stimuli that hyperactive children experience is not a crucial variable in their hyperactive behavior. Environmental stimulus reduction or enhancement in the classroom or at home appears to have no significant effect on such behavior. (Journal abstract modified)

001718 James, I. M.; Griffith, D. N. W.; Pearson, R. M.; Newbury, Patricia. Section of Clinical Pharmacology, Academic Department of Medicine, Royal Free Hospital, London NW3 2QG, England **Effect of oxprenolol on stage-fright in musicians.** Lancet (London). No. 8045:952-954, 1977.

The effect of 40mg oxprenolol on stage fright in 24 musicians was assessed in a double-blind crossover trial. Musical peformance judged by two professional assessors and by self-evaluation was found to improve. Greatest improvement was seen on the first performance and in those most affected by nervousness. Results indicate that the need for this drug for any individual would lessen with time. The efficacy of oxprenolol in the study is seen to bolster the case for using beta-adrenoceptor blocking drugs in normal subjects under acute emotional stress. 9 references. (Author abstract modified)

001719 Kales, Anthony; Kales Joyce D.; Jacobson, Allan; Humphrey, Frederick J., II; Soldatos, Constantin R. Sleep Research and Treatment Center, Pennsylvania State University, Milton S. Hershey Medical Center, Hershey, PA **Effects of imipramine on enuretic frequency and sleep stages.** Pediatrics. 60(4):431-436, 1977.

Four children with a history of primary enuresis were evaluated in both the sleep laboratory and at home in a 68 consecutive night protocol with successive conditions of 10 placebo baseline nights, 27 drug (imipramine) nights, and 31 placebo withdrawal nights. On the placebo conditions, two thirds of the enuretic events occurred during the first third of the night. Enuretic events occurred out of each sleep stage in approximate proportion to the time spent in that sleep stage for each third of the night. Thus, primary enuresis was found to be chiefly related to time of night and not any specific sleep stage such as stage 3 or 4 (slow wave) sleep. Administration of imipramine in a manner simulting clinical use of the drug resulted in a marked decrease in overall enuretic frequency. The reduction of enuretic frequency was not related to the effects of imipramine on sleep stages. There was a reduction of enuretic events in the first two thirds of the night with an increase in enuretic events in the last third of the night. These findings suggest that early in the night when sleep is deepest, imipramine decreases bladder excitability and/or increases the child's bladder capacity. This allows the child to continue to sleep without micturition and, later in the night when sleep is lighter, to be more aware of the stimuli from the bladder. Immediately following withdrawal of imipramine, enuretic frequency approximated baseline levels. Administration of imipramine resulted in a moderate degree of rapid eye movement (REM) suppression. With long-term administration, there was a dimunition of the REM suppressant effect. Initial withdrawal of imipramine produced a marked REM rebound. 13 references. (Author abstract)

001720 Kochansky, Gerald E.; Salzman, Carl; Shader, Richard I.; Harmatz, Jerold S.; Ogletree, Ann M. Psychopharmacology Research Laboratory, Massachusetts Mental Health Center, 74 Fenwood Rd., Boston, MA 02115 **Effects of chlordiazepoxide and oxazepam administration on verbal hostility.** Archives of General Psychiatry. 34(12):1457-1459, 1977.

The effects of chlordiazepoxide, oxazepam, and placebo on hostility, as both an inner motivational or potential state and verbal interpersonal behavior were compared. The findings relevant to the latter dimension of hostility are integrated with those findings, presented in an initial report, relevant to hostility as an inner motivational state. The verbal data again support the hypothesis that chlordiazepoxide induced increases in verbal interpersonal hostility, following frustration, are greater than those associated with placebo. With regard to oxazepam, the verbal hostility data were consonant with the motivational data that suggested that oxazepam does not substantially disinhibit hostility but did not as consistently differentiate oxazepam and chlordiazepoxide at the level of overt hostile behavior. 11 references. (Author abstract modified)

001721 Kupietz, Samuel S.; Winsberg, Bertrand G. Division of Child Psychiatric Research, Long Island Research Institute, New York State Department of Mental Hygiene **Caffeine and inattentiveness in reading-disabled children.** Perceptual and Motor Skills. 44(3, Part 2):1238, 1977.

Effect of caffeine on attentiveness in reading disabled children was investigated. Subjects were ten reading disabled boys from 9 years old to 11 years old. The effect of caffeine was assessed with an auditory vigilance task which is sensitive to psychostimulant drug effects. At 1 week intervals half the subjects were assessed by placebo followed by caffeine, and the other half were tested in reverse order. Caffeine was given in three 100mg NoDoz tables 1 hour before testing. Results showed that only the more hyperactive children tended to make fewer omissions under caffeine than under placebo, however, caffeine was not effective for attentional problems in this sample. 6 references.

001722 Labat, J.; Chuiton, J.; Bardon, A. no address **/Study of sultopride (LIN-1418) in agitated states./** Etude du sultopride (LIN 1418) dans les etats d'agitation. Psychologie Medicale (Paris). 9(1):171-182, 1977.

Effects of sultopride (LIN-1418) on psychomotor agitation of diverse etiology were examined. Analysis of the results of treatment of 22 patients with both psychic and motor agitation and associated dysthymia showed sultopride to be effective in controlling agitation. In contrast with other neuroleptics, its action on motor agitation is rapid, occurring within 3 days of commencement of treatment, but its action on psychotic agitation is slower. Sultopride is well tolerated by the cardiovascular system. Doses of neuroleptics given in association with sultopride may be reduced. The specific influence of sultopride and other neuroleptics on manic-depressive psychosis still remains to be clarified. 11 references. (Journal abstract modified)

001723 Mattila, M. J.; Palva, E.; Seppala, T.; Saario, I. Dept. of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Effects of trithiozine on psychomotor skills related to driving: a comparison with diazepam and interactions with alcohol.** Current Therapeutic Research. 22(6):875-885, 1977.

Effects of trithiozine, a new gastric antisecretory drug, on psychomotor skills related to driving were studied on paid healthy student volunteers. The effects of oral trithiozine, 200 and 400mg, alone and in combination with 0.5g/kg of ethyl alcohol, were compared in double-blind crossover trials against oral diazepam 10mg, alcohol 0.5g/kg, and lactose placebo. Reactive and coordinative skills, attention, flicker fusion, proprioception nystagmus, Maddox wing, and subjective estimations were included. The single dose trial with 12 volunteers revealed that neither trithiozine nor diazepam modified attention. Diazepam impaired reactive skills whereas coordinative skills remained largely uninfluenced by diazepam or trithiozine. Both trithiozine and diazepam impaired leg proprioception. In the multiple dose trial with 12 volunteers trithiozine 400 alone did not differ from placebo as to the coordinative skills, while both diazepam alone and trithiozine 400 in combination with alcohol impaired coordination somewhat more than alcohol did. It is concluded that trithiozine, having mild central sedative effects, usually lower and not higher than those of diazepam 10mg, could be a good and safe substitute of the combinations of anticholinergics and tranquilizers. 21 references. (Author abstract modified)

001724 Miletto, G. Service de Neuro-Psychiatrie de l'Hopital, Avenue Pasteur, F-13100 Aix-en-Provence, France **/Comparison of the effects of noctran 10 on hospitalized patients and patients treated at home./** Comparaison de l'effet du Noctran 10 chez les malades hospitalises ou a domicile en neuropsychiatrie. Psychologie Medicale (Paris). 9(1):165-170, 1977.

Comparison was made of the efficacy of the hypnotic noctran 10 in hospital treatment and with treatment in the home. Administration of noctran 10 to 50 hospitalized patients with neurotic, psychotic, or organic disorders, and to 100 patients treated at home indicated superior effect in the group treated in the home. The difference is minimal and not statistically significant, thus favoring the concept of the role of environment in sleep behavior. The drug is well tolerated, is not addictive, and is effective in low doses. Progressive quantitative reduction of dosage may begin once the patient is assured of the quality and stability of sleep. 7 references. (Journal abstract modified)

001725 Nagaraja, Jaya. no address **Clinical use of haloperidol (Serenace) in child psychiatry.** Child Psychiatry Quarterly (Hyderabad). 10(4):14-20, 1977.

To determine the efficacy of haloperidol (Serenace) in children, 160 children with either behavior disorder (temper tantrums, truancy, feeding disorder, sleep disturbance), acute anxiety, psychoneurosis (aphonia, hypochondriasis, functional fits, sleepwalking), or psychosis (mania, psychotic depression) were administered the drug over a 3 month period and observed for 3 months thereafter. Maximum cure rates were found in the behavior disorder and acute anxiety groups, with little or no change in the psychotic group. Psychoneurotics showed almost the same results in both drug and control groups, revealing the relative inefficacy of haloperidol with psychoneurotic children. It is concluded that haloperidol is effective in treating children with behavior disorder and acute anxiety.

001726 Parashos, A. J. Department of Psychiatry, Aristotelian University, Thessaloniki, Greece **The psilocybin-induced "state of drunkenness" in normal volunteers and schizophrenics.** Behavioral Neuropsychiatry. 8(1-12):83-86, 1977.

The effects of psilocybin, a psychomimetic substance, on mental functioning were investigated in normal and schizophrenic volunteers. The disturbances induced constituted a psychoneurotoxic syndrome, a state of drunkenness, of about 4 hours duration which developed in three distinct phases. The basic mental symptoms of this syndrome consisted of disturbances of the apperception, sensory perception, and emotion. A moderate impairment of ego functioning or reality appraisal and an inability to integrate different mental processes was observed. The psychomotor behavior was mainly harmonized to the prevailing emotional state and to the experiences caused by perceptual alterations. These changes were more severe in schizophrenics than in the normal subjects. From a psychopathological analysis of these changes it is concluded that the whole syndrome cannot be considered as related to the spontaneously triggered functional psychoses or to the organic ones, and therefore the term "model psychosis" is considered unsatisfactory. 23 references. (Author abstract modified)

001727 Pfefferbaum, Adolf; Darley, Charles F.; Tinklenberg, Jared R.; Roth, Walton T.; Kopell, Bert S. Psychiatry Service 116A3, Veteran's Administration Hospital, 3801 Miranda Ave., Palo Alto, CA 94304 **Marijuana and memory intrusions.** Journal of Nervous and Mental Disease. 165(6):381-386, 1977.

In an investigation of the effects of marihuana intoxication on memory function, 16 college educated male subjects were tested on free recall lists during intoxication with marihuana extract and during placebo conditions. On each testing day subjects studied six lists using a regular overt rehearsal procedure and six lists using an association overt rehearsal procedure in which they were to rehearse aloud both list items and associations to those items. Both marihuana and the association rehearsal procecure reduced the number of correct recalls and increased the number of intrusions. Results suggest that one of the effects of marihuana on cognitive functions in humans is to increase the number of intrusive thoughts and this may be the mechanism involved in some of the thought disorder observed with marihuana intoxication. 14 references. (Journal abstract)

001728 Rie, Ellen D.; Rie, Herbert E. Department of Psychology, Mather Memorial Building, Case Western Reserve University, Cleveland, OH 44106 **Recall, retention, and ritalin.** Journal of Consulting and Clinical Psychology. 45(6):967-972, 1977.

Effects of Ritalin were studied on 2 hour story recall, 2 day story retention, and 2 day changes on screening tests of achievement in a sample of 20 primary grade underachieving children. Subjects were of average intelligence and free of both demonstrable neurological impairment and major psychological problems. Comparisons of drug and no drug responses showed a significant positive drug effect on 2 hour story recall but not on 2 day story retention. A significant positive drug effect was also observed on achievement test scores after only 2 days when practice effects were discounted. The short time precluded skill acquisition. These findings indicate that immediate drug attributable gains in scholastic performance cannot be equated with ultimate gains in scholastic achievement. Immediate drug induced increments in test performance could be mistaken for long-term drug effects on achievement if baseline measures are obtained before

drug administration. Both baseline and ultimate functioning should be determined following drug administration. 16 references. (Author abstract)

001729 Saletu, Bernd. Sect. of Pharmacopsychiatry, Psychiatrische Universitatsklinik Wien, Wahringer Gurtel 74-76, A-1090 Wien, Austria **The evoked potential in pharmacopsychiatry.** Neuropsychobiology (Basel). 3(2-3):75-104, 1977.

Somatosensory, visual and auditory evoked potentials (EP) were recorded in different psychiatric populations before as well as during psychotropic drug treatment. Drug free schizophrenic patients showed shorter latencies, smaller amplitudes and an increased intraindividual variability in their EP than controls. Psychotic children but also children of schizophrenic mothers exhibited similar differences as compared to controls, suggesting a CNS overarousal as the pathoneurophysiological substrate of schizophrenia. Shorter latencies were also seen in children of psychopathic fathers. Regression and correlation analysis of psychopathological and EP measurements in hyperkinetic children revealed that: the shorter the latencies and the higher the amplitudes, the sicker was the child. During psychopharmacotherapy, significant changes occurred in the EP measurements, which were found to be significantly correlated with clinical improvement or deterioration. Neuroleptics induced a latency increase and an amplitude decrease in schizophrenic patients and psychotic children. Differences between therapy responsive and therapy resistant patients are described and, data concerning the role of the pretreatment EP as a predictor of therapeutic outcome are discussed. 118 references. (Author abstract)

001730 Schneider, E.; Ziegler, B.; Maxion, H. Zent. Neur. U. Neurochir., Abt. Neurologie, Klin. d. Johann-Wolfgang-Goethe-Universitat, Frankfurt/Main, Germany **Gamma-aminobutyric acid (GABA) and sleep: the influence of di-n-propylacetic acid on sleep in man.** European Neurology (Basel). 15(3):146-152, 1977.

The effects of di-n-propylacetic acid (DPA), an anticonvulsive drug, on sleep, has been investigated in 11 healthy volunteers using all-night sleep EEG recordings. DPA acts by an enhancement of the gamma-aminobutyric acid (GABA) level of the brain. Its influence on sleep seemed to be of interest on account of the metabolic relationship of GABA to other short chain fatty acids. After short-term application only a shortening of the time to fall asleep and of the waking time could be found, whereas under long-term administration a decrease in deep synchronous sleep could be observed. In contrast to the results known from animal studies no marked influence on REM sleep was observed. The action of DPA on sleep is similar to that of diphenylhydantoin. No so called matitudinal hangover could be revealed in either drug. 39 references. (Author abstract)

001731 Sheard, Michael H.; Marini, James L.; Giddings, Suzanne S. 34 Park Street, New Haven, CT 06508 **The effect of lithium on luteinizing hormone and testosterone in man.** Diseases of the Nervous System. 38(10):765-769, 1977.

Serum luteinizing hormone and testosterone were determined weekly during the course of a comparison of the effects of lithium versus placebo on impulsive aggressive behavior in 16 to 24-year-old male prisoners. The duration of drug treatment for each individual was up to 3 months. A significant reduction of serious aggressive behavioral incidents occurred in the third month on lithium and was accompanied by a significant rise in serum luteinizing hormone, with no change in serum testosterone. 29 references. (Author abstract)

001732 Sprague, Robert L.; Sleator, Esther K. Institute for Child Behavior and Development, University of Illinois, Champaign, IL 61820 **Methylphenidate in hyperkinetic children: differences in dose effects on learning and social behavior.** Science. 198(4323):1274-1276, 1977.

A study was undertaken which yielded differences in dose effects of methylphenidate (Ritalin) on learning and social behavior of 20 hyperkinetic children (mean age 8.3years). Results showed a peak enhancement of learning in children after being given a dose of 0.3milligram per kilogram of bodyweight, and a decrement in learning in those given larger doses. Social behavior showed the most improvement in children given 1.0milligram per kilogram. These results had been hypothesized from theoretical dose response curves which indicate different target behaviors would improve at different doses. 21 references. (Author abstract modified)

001733 Stillman, Richard C.; Wolkowitz, Owen; Weingartner, Herbert; Waldman, Ivan; DeRenzo, Emil V.; Wyatt, Richard Jed. Intramural Research Program, National Institute on Drug Abuse, Rockville, MD 20852 **Marijuana: differential effects on right and left hemisphere functions in man.** Life Sciences (Oxford). 21(12):1793-1799, 1977.

A series of experiments is reported investigating the possibility of differential effects on the right and left hemispheres by marihuana in normal right-handed marihuana users. It was found that marihuana, smoked at moderate doses, produced a differential impairment of the reaction times of right-handed males to pictorial stimuli presented to the left and right cerebral hemispheres. After smoking marihuana responses to pictorial stimuli presented to the right hemisphere were slowed significantly less than to the left hemisphere. Responses to verbal stimuli (trigrams) were slowed equally in both hemispheres, preserving an initial left hemisphere superiority for this material. This suggests that marihuana may differentially change the processing speed or relative dominance of man's two cerebral hemispheres, depending on the nature of the material being processed. 13 references. (Author abstract modified)

001734 Touyz, S. W.; Beumont, P. J. V.; Saayman, G. S.; Zabow, T. Dept. of Psychology, University of Cape Town, Rondebosch, South Africa **A psychophysiological investigation of the short-term effects of clozapine upon sleep parameters of normal young adults.** Biological Psychiatry. 12(6):801-822, 1977.

A nine consecutive night, double-blind design was used to assess the effects of a psychotropic agent (clozapine) upon sleep parameters as well as measures of mood and performance in a group of seven normal young adults. Placebo was administered to a control group of seven subjects. EEGs and EOGs were monitored throughout the night in a laboratory environment and were scored according to standardized criteria. The administration of 25mg clozapine/night for three consecutive nights significantly reduced stage 4 sleep on the second and third nights. Whereas stage REM sleep was not affected, a variety of REM indices were significantly increased on the third night of clozapine administration and/or on the first night of clozapine withdrawal. The number of body movements and the number of body movements/minute of sleep were significantly reduced on the three nights of clozapine administration. Numerous psychophysiological side-effects were reported. These results indicate that clozapine may be a useful medication in the treatment of sleep disorders. However, the incidence of adverse side-effects represents a major limitation in the use of clozapine as an hypnotic agent at the dose rate employed. 36 references. (Journal abstract)

001735 Velasco, M.; Velasco, F.; Almanza, X.; Munoz, J.; Olvera, A. Division of Neurophysiology, Scientific Research Department, National Medical Center, I.M.S.S., Mexico, D.F. (73-032) **Effect of dextroamphetamine on somatic evoked potential components in man with special reference to talk relevance and selective attention.** Neuropharmacology (Oxford). 16(12):819-825, 1977.

The effect of a single dose of 40 to 50mg of dextroamphetamine (DXA) on early and late components of the somatic evoked potentials (SEP) was analyzed in a group of normal volunteers under different conditions of task relevance and selective attention. Concomitant effects of amphetamine on level of general alertness were evaluated by changes in EEG, EKG and respiration frequencies and effect of amphetamine on overall performance of subjects by a series of psychological tests practiced pre/postdrug. Dextroamphetamine significantly decreased the amplitude of the late P5a component during distraction and inattentive conditions while it did not significantly change either the amplitude of the early P3a component or the latency of all components of SEP. In addition, amphetamine significantly increased EEG, EKG and respiration frequencies under some conditions, and decreased reaction time and scores of the visual retention test of Benton. These results suggest that amphetamine affects propioceptive transmission and integration at a nonspecific descending corticothalamic system mediating late SEP components rather than at the specific ascending lemniscal system mediating early SEP components. The decreasing effect of amphetamine on late SEP components may be due either to an increased level of general alertness or to selective attention blocking irrelevant afferent stimuli or both. On the contrary, the decreasing effect of amphetamine on reaction time may be due to a facilitation of the motor process, independent of the sensory one, involved in single and discrimination response conditions. 11 references. (Author abstract)

001736 Winstead, Dan K.; Parker, Michael; Willi, Franz J. P. VA Hospital, 1601 Perdido St., New Orleans, LA 70146 **Propoxyphene on demand: analgesic-seeking behavior in psychiatric inpatients.** Archives of General Psychiatry. 34(12):1463-1468, 1977.

A study which attempts to evaluate factors associated with analgesic use among psychiatric inpatients is presented, and the hypothesis that anxiety, other measures of psychopathology, and ward tension are associated with frequent analgesic use was tested. Although anxiety is known to enhance a patient's response to pain, the exact relationship is unclear. This problem is particularly acute among psychiatric patients where analgesics are frequently both used and abused. An unselected series of psychiatric admissions during a three month period were administered the State/Trait Anxiety Inventory, MMPI, and a questionnaire dealing with prior drug use. Propoxyphene napsylate (Darvon-N) was made freely available on request from nurses who recorded details of the interaction on a prepared card. The nursing staff also recorded unusual incidents on the unit and evaluated daily the level of ward tension. The results indicate that, when made freely available to psychiatric inpatients, propoxyphene was used very conservatively and for appropriate complaints. Factors associated with drug seeking behavior are discussed in relation to other research regarding the use and abuse of analgesics. 44 references. (Author abstract modified)

001737 Wolfensberger-Haessig, Chr. Postfach, CH-8803 Ruschlikon, Switzerland /**"Persisting infantile pattern of attentiveness" in backward school children with brain dysfunction. Attempt of a human ethologically oriented interpretation and its therapeutic application./** Die "persistierende kleinkindliche Aufmerksamkeitsform" hirndysfunktionell behinderter Schuler. Versuch einer humanethologisch orientierten Interpretation und ihre therapeutische Anwendung. Therapeutische Umschau (Revue Therapeutique) (Bern). 34(1):15-20, 1977.

The defect in attention in children with minimal brain dysfunction is discussed. In minimal brain dysfunction there is retardation of maturity of cortical functions controlling the innate phylogenetically old patterns of social and emotional behavior. It is recommended that children with this attention deficit be treated with methylphenidate, to which these children respond very well, and be educated in small classes of four, or at most five, other children with minimal brain dysfunction. 4 references.

15 TOXICOLOGY AND SIDE EFFECTS

001738 Abiuso, Patrick D.; Pandarinath, S. Cooper Medical Center, Camden, NJ **Methylphenidate (Ritalin) abuse.** Journal of the Medical Society of New Jersey. 74(12):1061-1062, 1977.

A case of methylphenidate (Ritalin) abuse in a patient on a methadone program for narcotic withdrawal is reported. Complications of foreign body granulomata, osteomyelitis, pulmonary hypertension, and embolization are discussed. The possibility of granulomata occurring on heart valves should be kept in mind, and these patients should be examined carefully for evidence of bacterial endocarditis. It is suggested that certain diagnostic and laboratory procedures such as pleural biopsy will aid in early diagnosis. 9 references. (Author abstract)

001739 Albanese, Helen; Gaarder, Kenneth. University of Texas Health Science Center, 7703 Floyd Curl Dr., San Antonio, TX 78284 **Biofeedback treatment of tardive dyskinesia: two case reports.** American Journal of Psychiatry. 134(10):1149-1150, 1977.

Two case reports of biofeedback treatment of tardive dyskinesia are reported in which two well motivated and intelligent patients learned to control their mouth movements. A general reduction of tension was experienced by both patients, and both gave reports of increased well-being. Since spontaneous remission occurs in tardive dyskinesia, it cannot be proven that the biofeedback treatment was responsible for the marked improvement of these patients. 5 references.

001740 Allen, R. Michael. El Paso Regional Academic Health Center, El Paso, TX **Tardive dyskinesia: a preventive approach.** Current Therapeutic Research. 22(6):914-917, 1977.

A theoretical approach is proposed for the prevention of tardive dyskinesia, considered the most serious complication of neuroleptic therapy for schizophrenia. The mechanism of tardive dyskinesia is traced to a relative dopaminergic hyperfunction in the corpus striatum, attributable either to a pure denervation or permanent structural or ultrastructural damage to the postsynaptic receptors or cells. Studies of amantadine hydrochloride in the treatment of tardive dyskinesia are reviewed, and it is argued that amantadine has beneficial effects in preventing dyskinesia. It is concluded that amantadine should be used in the treatment of drug induced extrapyramidal disorder, and in high-risk patients whether or not they have such disorder as a potential prophylaxis against the development of tardive dyskinesia. 12 references.

001741 Alpert, Murray; Diamond, Florence; Kesselman, Martin. Lillhauser Laboratories, Dept. of Medicine, NYU Medical School, 550 First Avenue, New York, NY 10016 **Correlation between extrapyramidal and therapeutic effects of neuroleptics.** Comprehensive Psychiatry. 18(4):333-336, 1977.

The correlation between extrapyramidal signs and the therapeutic effects of neuroleptics was investigated. During the first weeks of treatment in a homogenous (for age, sex and chronicity) group of schizophrenics, a fixed dose incremental schedule of trifluoperazine was followed. Extrapyramidal effects were measured through quantitative analysis of digital tremor. Treatment response was measured after 4 weeks of medication. Evidence developed suggests that patients who show a better treatment response are less vulnerable to extrapyramidal effects. A number of methodological issues, placing restraints on the generalization of the data, are discussed. 10 references. (Author abstract modified)

001742 Amsler, H. A.; Teerenhovi, L.; Barth, E.; Harjula, K.; Vuopio, P. Biological and Medical Research Division, Sandoz Ltd., CH-4002 Basel, Switzerland **Agranulocytosis in patients treated with clozapine: a study of the Finnish epidemic.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(4):241-248, 1977.

The occurrence of a sudden outbreak of agranulocytosis in Finland among patients being treated with clozapine was investigated to find a local precipitating factor. Granulocytopenia after clozapine was found to have the same characteristics as that reported after phenothiazines. No local factor, either genetic or environmental, was found which could have been responsible for the increased frequency of occurrence in Finland. The need to be aware of the risk and to take appropriate precautionary measures (e.g. weekly leucocyte counts in the first months) is emphasized. 8 references. (Author abstract)

001743 Ananth, J. V.; Klingner, A.; Ban, T. A.; Lehmann, H. E. Department of Psychiatry, McGill University, Montreal, Quebec, Canada **Sex differences in response to drug treatment.** Indian Journal of Psychiatry (Poona). 19(2):82-86, 1977.

Sex differences in response to drug treatment were investigated in a review of comparative studies on psychopathology, response to drug administration, and drug withdrawal. It is indicated that female patients manifested more severe psychopathology, a greater capacity to tolerate drug withdrawal without serious side-effects, and a higher incidence of skin pigmentation in adverse reactions. The difference in skin pigmentation as an adverse reaction points to the possibility of overproduction of hydroxychlorpromazine in females, lending some support to sex differences in drug metabolism. A difference was also found in the dosage of medication between males and females due to poorer response to drug treatment. 35 references.

001744 Ananth, J.; Nanci, T. Department of Psychiatry, St. Mary's Hospital, Montreal, Quebec, Canada **Adverse reactions to medication in psychiatric inpatients: their meaning, utility and problems.** Psychiatric Journal of the University of Ottawa (Ottawa). 2(3):138-142, 1977.

An adverse reaction monitoring program in a hospital psychiatric ward is described. Adverse reactions of patients in the study were collected daily from ward rounds, interviews with patients, doctors, and nurses, and laboratory reports. Medications in the study included neuroleptics, antidepressants, antiparkinsonian agents, anxiolytics, and hypnotics. Results showed 400 adverse reactions in 75 patients, confirming that adverse reactions are extremely common. Types of reactions included nervous system and psychiatric reactions, gastrointestinal reactions, extrapyramidal signs, and abnormal laboratory findings. None of the reactions were severe enough to cause transfer to a medical ward, and most of the side-effects dissipated without countermeasures. Most side-effects occurred during the first week, indicating the need for careful initial observation; 19% of the side-effects did not dissipate and remained as a source of discomfort and annoyance to the patients. 12 references.

001745 Aronow, R.; Miceli, J. N.; Done, A. K. Dept. of Pediatrics, Wayne State University School of Medicine, Detroit, MI 48201 **Observations on the treatment of phencyclidine (PCP) poisoning.** Clinical Toxicology. 10(4):470, 1977

Paper presented at the joint meeting of the American Academy of Clinical Toxicology, the American Association of Poison Control Centers, and the Canadian Academy of Clinical Toxicology, Seattle, 1976, reported pharmacokinetic studies performed in patients who had overdosed themselves with the currently popular street drug phencyclidine (PCP). Data are presented on the serum half-life, gastrointestinal drainage levels, peritoneal clearance, and suggested treatment. (Journal abstract modified)

001746 Aschoff, J. C.; Becker, W.; Jurgens, R. Neurologische Ambulanz der Universitat, Steinhovelstr. 9, D-7900 Ulm, Germany **/Computer oculographic double blind study of changes in vigilance: alprenolol versus diazepam./** Computer-okulographische Doppelblindstudie zur Erfassung von Vigilanzanderungen: Alprenolol -- Diazepam. Medizinische Welt (Stuttgart). 28(35):1403-1406, 1977.

A computerized oculographic technique was used to determine the changes in vigilance caused by diazepam and alprenolol. All drugs that have a fatigue side-effect lower attention and reactivity, and their effect on a patient's behavior in traffic should be tested. Reduction in the rate of saccadic eye movements indicates lowered vigilance and thus increased risk of traffic accidents. Because the sedative effect of diazepam has been reported, a double-blind study was made of the effects of diazepam, alprenolol and placebo on saccadic eye movements. A test of 12 patients showed that alprenolol does not decelerate ocular motion and does not change reaction rates when compared to placebo. It is concluded that any central effects of alprenolol do not affect vigilance or reactive behavior. 14 references.

001747 Asnis, Gregory M. Long Island Research Institute, Central Islip, NY 11722 **Tardive dyskinesia: is it or is it not? A review of the problems in diagnosis and a case study.** Diseases of the Nervous System. 38(10):856-859, 1977.

A differential diagnosis which exemplifies the importance and problems of diagnosis of tardive dyskinesia is presented. The case study illustrates that hysteria must not be neglected as an etiology of dyskinetic movements similar to tardive dyskinesia. It is suggested that dyskinetic symptoms secondary to hysteria may be becoming more common as greater numbers of psychiatric patients with tardive dyskinesia appear on psychiatric wards and are treated as special patients for their unusual disorder. In the case of neuroleptic treatment of a suspected patient with tardive dyskinesia, it is suggested that medication be lowered or stopped if the psychiatric condition permits or changed to an alternate therapy to allow for evaluation and to possibly prevent an irreversible state from forming. 24 references.

001748 Bozza-Marrubini, M.; Frigerio, A.; Ghezzi, R.; Parelli, L.; Restelli, L.; Selenati, A. Centro Antiveleni Ospedale Maggiore, Milan, Italy **Two cases of severe orphenadrine poisoning with atypical features.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):137-152, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, two atypical cases of severe orphenadrine poisoning are reported. Of eight such cases admitted to the Milan Poison Control Center with typical symptoms of coma, convulsions, mydriasis, tachycardia and postcoma hallucinations, two cases indicated that the toxic reaction also resulted in severe heart, lung and liver distress. Subsequently, 21 case histories of severe orphenadrine poisoning which resulted in 15 deaths were examined to confirm the possibility that the drug is cardiotoxic. Data from all cases led to the following observations in the treatment of orphenadrine intoxication: 1) heart activity should be monitored by ECG continuously and cardiac resuscitation equipment should be made immediately available; 2) convulsions should be sedated; 3) hypoxia should be corrected; 4) the liver function should be followed closely, and 5) gastric lavage should be performed as soon as possible. It is noted that physostigmine salicylate appears to cause striking improvement in coma and hallucination symptoms. 26 references.

001749 Budhiraja, R. D.; Bala, S.; Garg, K. N. Department of Pharmacology, Medical College, Rohtak, Punjab, India **Effect of dietary factors on drug action.** Clinician (Panjim-Goa). 41(7):257-264, 1977.

A brief overview is presented of the effects of dietary factors on drug action in humans. Various dietary factors which may have a pronounced effect on the therapeutic activity of a number of drugs are: 1) presence or absence of food in the gastrointestinal tract; 2) the use of alcoholic beverages, particularly with psychoactive drugs; 3) gastric and urinary pH; 4) nutritional deficiencies; and 5) foods containing specific chemicals such as tyramine which can lead to fatal or harmful reactions with monoamine oxidase inhibitors. 57 references.

001750 Burns, C. R. National Society on Alcoholism and Drug Dependency, Wellington, New Zealand **Chlormethiazole (hemineurin).** New Zealand Medical Journal (Dunedin). 589(85):489, 1977.

The use of chlormethiazole (hemineurin) as the drug of choice in the treatment of withdrawal symptoms likely to occur following a period of high alcohol consumption is deplored in a letter to the editor because of the drug's highly addictive nature. It is suggested that alcohol withdrawal symptoms treated with chlormethiazole are usually mild, while those resulting from prolonged use of chlormethiazole are severe. It is concluded that while chlormethiazole may prove useful as a night treatment for psychogeriatric patients, it should not be used on an inpatient or outpatient basis in the treatment of the alcoholic or any patient addicted to sedative drugs.

001751 Burrows, G. D.; Vohra, J.; Dumovic, P.; Maguire, K.; Scoggins, B. A.; Davies, B. Dept. of Psychiatry, University of Melbourne, Parkville, Vic. 3052, Australia **Tricyclic antidepressant drugs and cardiac conduction.** Progress in Neuro-Psychopharmacology. 1(3/4):329-334, 1977.

Clinical and experimental data are presented on the effect of tricyclic antidepressants respectively in vivo on the cardiac conduction in man, and in vitro on the isolated perfused guinea-pig heart. Distal intracardiac conduction defects have been observed in patients ingesting both toxic and therapeutic doses of either nortriptyline, imipramine or amitriptyline. In a crossover comparative study of doxepin and nortriptyline (150mg/day 3 weeks), six out of 17 patients on nortriptyline and only one patient on doxepin showed distal intracardiac conduction effects. Plasma levels of doxepin (46 to 59ng/ml) were lower than those of nortriptyline (167 to 225ng/ml). The in vitro study of tricyclic antidepressants showed that the tricyclics for six experiments all decreased the force of contraction of the heart in comparison to control injections of a buffer solution. It is concluded that the distal intracardiac conduction defects caused by tricyclics in toxic and therapeutic doses may explain the sudden deaths reported with tricyclic antidepressants. The isolated perfused guinea-pig heart is considered an efficient toxicological model for testing and treating drug induced cardiac arrhythmias. 21 references. (Author abstract modified)

001752 Buysschaert, M.; Mahieu, P.; Hassoun, A.; Col., J.; Reynaert, M; Tremouroux, J. Departement de Medecine Interne, Cliniques Universitaires St. Luc, avenue Hippocrate 10, B-1200 Bruxelles, Belgium **About a non-fatal massive intoxication with sustained-release thioridazine. Clinical and therapeutic problems.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):153-162, 1977.

In a paper presented at the 7th International Congress of the European Association of Poison Control Centres, held at Oslo, Norway during June 1976, clinical and therapeutic problems in the treatment of a massive intoxication with sustained release thioridazine are discussed. A case report of a female, 27-year-old patient who had ingested approximately ten grams of phenothiazine illustrates the necessity of employing an endocardial pacemaker when excitability disturbances are associated with conduction disturbances. The toxicological profile of the patient is discussed and compared to that of patients suffering from intoxication with ordinary thioridazine. 14 references

001753 Casarino, John P. St. Vincent's Hospital and Medical Center of New York, 153 West 11th St., New York, NY 10011 **Neuropathy associated with amitriptyline: bilateral footdrop.** New York State Journal of Medicine. 77(13):2124-2126, 1977.

A case report of neuropathy associated with amitriptyline is presented, in which a 66-year-old woman developed bilateral foot drop and subjective numbness of both feet without sensory impairment to pain, touch, position, or vibration. Although no descriptions of individual case reports of footdrop associated with amitriptyline therapy have appeared in the American literature, the existence of two additional cases of footdrop and four cases of peripheral neuropathy involving median and peroneal nerve distributions is reported. Initial evidence indicates that the reactions are reversible; nevertheless, the variability of the rates of recovery and the absence of objective clinical data documenting the recoveries suggest the need for closer clinical monitoring in this area. 6 references.

001754 Casey, Daniel E.; Denney, Duane. Dept. of Psychiatry, Veterans Administration Hospital, Portland, OR 97207 **Pharmacological characterization of tardive dyskinesia.** Psychopharmacology (Berlin). 54(1):1-8, 1977.

A hypothesis concerning a pharmacological causative mechanism for tardive dyskinesia (TD) was investigated, suggesting that tardive dyskinesia may be a clinical manifestation of a relative imbalance between the inversely related dopaminergic (DA) and acetylcholinergic (ACh) influences in the central nervous system (CNS). Six patients were evaluated

with single challenge doses of a DA agonist, levodopa, and antagonist, droperidol, as well as with an ACh agonist, physostigmine, an antagonist, benztropine, and a placebo. A single blind trial with deanol and placebo followed. Responses, measured by an electrophysiological technique, formed two subgroups. The patients who improved with a DA antagonist or an ACh angonist improved while taking deanol. Another group of patients were made worse with a DA antagonist or ACh agonist and were worsened or had no response while taking deanol. While the results add support to the concept of counterbalancing DA/ACh influences in TD, further investigaton of TD subtypes and predictors of drug response is warranted. 44 references. (Author abstract modified)

001755 Cervi-Skinner, Sergio J. Veterans Administration Hospital, Roseburg, OR **Lithium-carbonate-induced hypercalcemia.** Western Journal of Medicine. 127(6):527-528, 1977.

A case of hypercalcemia in a 63-year-old manic-depressive male following 14 months treatment with lithium carbonate (600mg twice daily) is reported. Fourteen months following initiation of treatment the patient presented with hyperactivity and irritability, loss of memory, insomnia, aggressiveness, confusion and disorientation, increased thirst and constipation. All tests were within normal levels except for serum calcium level. Discontinuation of lithium therapy resulted in a decrease in serum calcium. With the recurrence of manic symptoms and reinstitution of lithium treatment, serum calcium levels again increased. Inappropriately high serum parathyroid levels suggested a possible loss of feedback mechanism. It is suggested that all patients receiving lithium carbonate therapy be closely monitored for hyperparathyroidism and hypercalcemia. 2 references.

001756 Challis, R. E.; Scopes, J. W. Pediatric Unit, St. Thomas's Hospital Medical School, London SE1 7EH, England **Late withdrawal symptoms in babies born to methadone addicts.** Lancet (London). No. 8050:1230, 1977.

Two cases illustrating late development of withdrawal symptoms in neonates born to heroin addicts switched to methadone maintenance during the pregnancy are reported in a letter to the editor. In the first infant, born to a woman on 40mg daily of methadone throughout pregnancy, irritability, weight loss, and hyperactivity manifested on the seventh day following birth, and chlorpromazine was required for seven days. The second infant, born to a woman who had taken 80mg heroin and 60mg methadone for the first 5 months of pregnancy and who had reduced intake to 20mg methadone for the remainder of the pregnancy, showed hyperactivity and sneezing on the fourth day postpartum and static weight by the sixth day. Reduction of the chlorpromazine dose on the eleventh day resulted in a generalized convulsion. Differences in the pharmacokinetics of heroin and methadone may explain the later withdrawal symptoms found in infants born to methadone addicts. The importance of close observation of these children for at least the first seven days of life is emphasized. 2 references.

001757 Chambers, G.; Kerry, R. J.; Owen, G. Northern General Hospital, Sheffield, England **Lithium used with a diuretic.** British Medical Journal (London). No.6090:805-806, 1977.

Although the combined use of lithium salts and diuretics has been said to be contraindicated, a case report is present of the successful long-term treatment of a manic/depressive patient with lithium carbonate, and the eventual development and treatment of a diabetes insipidus like state with bendrofluazide. Clinicians prescribing a diuretic to a patient on long-term lithium should bear in mind the following: 1) fairly close laboratory control of the serum lithium concentration is required, possible as an in-patient; 2) an immediate increase in the serum lithium concentration should be anticipated; and 3) restabilization may be at a lower lithium dose. 5 references.

001758 Christensen, K. Norregaard; Andersen, H. Harrestrup. Department of Anaesthesia, Odense University Hospital, Odense, Denmark **Deliberate poisoning with tricyclic antidepressants treated in an intensive care unit.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):511-515, 1977.

At the International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, a retrospective survey of 158 patients treated during a 5 year period for tricyclic antidepressant intoxication at an intensive care unit in Odense, Denmark is presented, and treatment objectives are described. Statistics concerning age and sex of patients, average dosage taken by patients, number of patients per year, polydrug intoxication, and frequency of therapeutic complications are presented. Typically, therapy consisted of stomach aspiration, a 24 hour diuresis, and an attempt to obtain mild alkalization by the intermittent use of infusion of isotonic sodium bicarbonate solution. All other treatment was symptomatic.

001759 Clark, Stephen Jack. University of Utah **An automated system for the prediction and prevention of adverse drug reactions. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-18732 HC$15.00 MF$8.50 179 p.

A drug monitoring system with potential to detect most of the predictable adverse drug reactions is described, and the extent to which pharmacokinetic monitoring of digoxin therapy can increase the accuracy of predicting serum drug concentration is discussed. The system includes a high level automated medical decision-making tool and a rapidly accessible patient oriented medical base. The prediction of potentially hazardous adverse reactions is specific for the individual and based on all available information to fully characterize the disease state and therapeutic regimen. The data base consists of 112 pharmacotherapeutic decision-making sectors of known clinically significant adverse reactions. Each sector may monitor from 1 to 100 or more individual drugs. Experience to date suggests that pharmacokinetic monitoring provides a means of predicting serum drug concentration, but it has not been found clinically significant for routine automated drug monitoring because of incomplete preadmission drug histories and the large interpatient and intrapatient variability in pharmacokinetic variables. (Journal abstract modified)

001760 Cohn, Cal K. Department of Psychiatry, University of Texas Medical School at Houston, PO Box 20708, Houston, TX 77030 **Lithium.** Texas Medicine. 73(10):73-75, 1977.

A review of lithium, its uses, mechanisms, side-effects, and interactions with drugs and other medical conditions, is presented. Lithium is indicated in treatment of acute mania, prophylaxis of recurrent mania, hypomania, recurrent depressive disorders, and in the prevention of recurrent episodes of schizoaffective schizophrenia. Side-effects which are briefly discussed include nontoxic goiters, hypothyroidism, polyuria, and diarrhea. The use of serum lithium levels in monitoring lithium therapy is explored. Furthermore, lithium is discussed in relation to leukocytosis, low salt diets and diuretics, electrocardiographic changes, mood, dermatitis, pregnancy, and organic brain syndrome. 9 references.

001761 Cowan, G. O. British Military Hospital, Munster, B.F.P.O. 17, Germany **Bromocriptine and gastric acid output.** Lancet (London). No. 8008:425, 1977.

Since nausea, peptic ulcer, and gastrointestinal hemorrhage are side-effects in bromocriptine therapy for parkinsonism, the effect of bromocriptine on gastric acid output was measured in nine male volunteers 18 to 35 years old. Gastric juice was collected for 1 hr through a nasogastric tube and then 2.5mg bromocriptine in 20ml water was instilled down the nasogastric tube. After 15 min gastric juice was collected every 15 min for 1 hr. Mean gastric acid output increased from 0.37mM/15 min to 1.05mM/15 min. This side effect of bromocriptine does not seem to be related to the dopaminergic effect of bromocriptine. 6 references.

001762 Crane, George E. North Dakota State Hospital, Jamestown, ND **Prevention of tardive dyskinesia.** Current Psychiatric Therapies. 17:227-234, 1977.

The cause of and preventive measures against tardive dyskinesia are discussed. It is pointed out that although evidence is overwhelming that tardive dyskinesia is the result of excessive use of neuroleptics in the treatment of psychoses, the psychiatric community has not responded to this knowledge by more careful monitoring of adverse reactions in psychotic patients or by seeking a change in psychotic management through the use of these drugs. Suggestions on taking drug histories, and initial and subsequent examinations, which would concentrate on a close monitoring of patients in order to detect extrapyramidal disorders in their initial stages are discussed. An overview of current practices in drug therapy in mental illness is presented, and precautionary measures are suggested for both therapy in the acute phase and for maintenance therapy which may reduce the risk of tardive dyskinesia. Recommended dosage ceilings are presented for chlorpromazine therapy. Management techniques for the patient who has symptoms of tardive dyskinesia are discussed. 22 references.

001763 Crome, P.; Dawling, S.; Braithwaite, R. A.; Masters, J.; Walkey, R. Poisons Unit, Guy's Hospital, London SE1, England **Effect of activated charcoal on absorption of nortriptyline.** Lancet (London). No. 8050:1203-1205, 1977.

To examine the adsorptive capacity of a new effervescent activated charcoal preparation (medicoal) for nortriptyline, a series of in vivo and in vitro studies was undertaken. A single dose of the effervescent charcoal 30 min after a dose of 75mg nortriptyline produced a 60% mean reduction in both peak plasma levels and nortriptyline availability in healthy volunteers. Multiple doses of the effervescent charcoal produced 70% mean reduction in peak nortriptyline levels and availability. Activated charcoal is recommended for the treatment of tricyclic antidepressant poisoning. In in vitro tests, a 10g packet of the effervescent preparation containing 5g activated charcoal had an adsorptive capacity of approximately 3000mg nortriptyline, a dose not usually exceeded in most cases of trycyclic antidepressant overdose. 18 references. (Author abstract modified)

001764 Crome, Peter; Higgenbottom, T.; Elliott, J. A. Guy's Hospital, London SE1 9RT, England **Severe meprobamate poisoning: successful treatment with haemoperfusion.** Postgraduate Medical Journal (Oxford). 53(625):698-699, 1977.

Treatment of severe meprobamate poisoning with hemoperfusion in a 56-year-old woman with a long history of depression is briefly reported. Charcoal hemoperfusion used to treat a very large overdose of meprobamate was followed by full recovery. The plasma clearance of meprobamate was 153 ml/min and this compares favorably with values obtained for hemodialysis. The indications for hemoperfusion are reviewed. 9 references. (Author abstract modified)

001765 Cutler, Neal R.; Anderson, Douglas J. University of California at Irvine, Long Beach, CA 90822 **Proven asymptomatic eosinophilia with imipramine.** American Journal of Psychiatry. 134(11):1296-1297, 1977.

The clinical confirmation of the correlation between imipramine treatment and asymptomatic eosinophilia in the case of a 57-year-old male suicide attempt was reported. A diagnosis of psychotic depression was made, the patient was started on 75mg of imipramine, increased over the next few days to 300mg/day. On the 12th hospital day, the patient developed coughing with chest pain. An examination of his blood revealed a total eosinophil count of 10,750 (45% of the total white count). Although pulmonary symptoms and physical findings resolved quickly, the eosinophilia persisted and increased to a maximum of 66% of the total white count. After imipramine discontinuation, leukocytes and eosinophils fell to normal levels within 16 days. Experimental tolerance testing of the patient on low doses of imipramine for a month again caused a rise in eosinophil count, but to lower levels than previously. The data appear to confirm the suspicion that asymptomatic eosinophilia can be caused by imipramine and that desensitization can occur. 4 references.

001766 Dainow, Ivor I. Medical Department, Brocades Ltd., West Blyfleet, Surrey KT14 6RA, England **Deaths after overdoses of orphenadrine.** Lancet (London). No. 8039:664, 1977.

In a letter to the editor, the distinction between the effective dose and the lethal dose of orphenadrine, an agent used to counteract extrapyramidal side-effects due to administration of the phenothiazines, is discussed. A potentially lethal interaction between orphenadrine and phenothiazine is discussed and attributed to careless pharmaceutical or medical distribution of the drug. It is suggested that the denial to a large number of patients of the benefits of orphenadrine because a minority may misuse it is not the solution to the problem.

001767 Dam, Willy; Klysner, Anne-Marie. Bispebjerg Hospital, Copenhagen, Denmark **Respiratory complications in patients with intoxication.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):40-47, 1977.

In a paper presented at the 7th International Congress of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, the treatment of respiratory complications in patients intoxicated by drugs including tricyclic antidepressants, phenothiazine, and antiparkinson agents, is described. Criteria for admittance of poisoned patients to the intensive therapy unit of the Bispebjerg Hospital include: 1) respiratory insufficiency, 2) need for hyperventilation therapy, and 3) likelihood of convulsions. The use of artificial ventilation with patients intoxicated by tricyclic antidepressants and in patients with slightly increased intracranial pressure is discussed, and the use of special ventilation techniques for patients intoxicated by gluthetimide and meprobamate is described.

001768 Dekret, Jeffrey J.; Maany, Iradj; Ramsey, T. Alan; Mendels, Joseph. Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA **A case of oral dyskinesia associated with imipramine treatment.** American Journal of Psychiatry. 134(11):1297-1298, 1977.

A causal relationship between imipramine treatment and an oral dyskinesia was demonstrated in the case of a 52-year-old man hospitalized for depression and guilt ruminations. The patient had been taking haloperidol prescribed during hospitalization 6 months before, and had been treated with methyldopa and hydrochlorothiazide for hypertension. The patient was removed from medications until the fourth week in hospital, when imipramine was started and increased to a dosage of 250mg/day. Soon after the maximum dosage was started, the patient developed abrupt involuntary buccal contractions and other symptoms of oral dyskinesia that disturbed his speech and sleep and caused mouth ulcerations. Although the relationship of the dyskinesia to imipramine was recognized, the dosage was reduced rather than eliminated. Two weeks later, on lower dosages of imipramine, most dyskinesia disappeared. The dyskinesia reappeared with another increased dosage, but was less severe. The patient was discharged on a lowered dosage, and the dyskinesia disappeared and did not recur. It is hypothesized that supersensitivity of dopamine receptors may develop following prolonged blockade of receptors by neuroleptics leading to relative hyperdopaminergic and hypocholinergic imbalance in the basal ganglia. 5 references.

001769 Dolara, P.; Franconi, F. Instituto di Farmacologia dell 'Universita' Firenze, Florence, Italy. **Hypertonic sodium chloride and lidocaine in a case of imipramine intoxication.** Clinical Toxicology. 10(4):395-398, 1977.

Control of cardiac arrhythmia in imipramine intoxication in a child by the combined use of hypertonic sodium chloride and lidocaine is described. A 6-year-old boy, previously treated with imipramine for enuresis, ingested 1 gram of imipramine tablets. Treatment with hydrocortisone (200mg) and infusion of 0.1% norepinephrine to control severe hypotension resulted in the development of ventricular tachycardia. Pyridostigmine i.m. and intravenous infusion of NaCl did not control the tachycardia. Addition of 1% lidocaine to the continued infusion of NaCl (total 60meq Na) reverted the ventricular tachycardia within a few minutes. Results suggest that extracellular sodium concentration may be a critical factor in correction of myocardial toxicity of tricyclic antidepressants. 16 references.

001770 Ducomb, Laurence; Baldessarini, Ross J. no address **Timing and risk of bone marrow depression by psychotropic drugs.** American Journal of Psychiatry. 134(11):1294-1295, 1977.

A case of bone marrow depression caused by psychotropic drug administration is presented. A 21-year-old male developed an acute psychotic illness characterized by agitation, gradiosity, paranoid delusions, and auditory hallucinations. In the second month of treatment with haloperidol, he developed motor restlessness and markedly deteriorated mental status. Thioridazine and chlorpromazine medications were sequentially added. A repeated leukocyte count in the patient showed an extremely low white blood cell count, with no granulocytes in peripheral blood and a hypoplastic iliac bone marrow containing some myeloblasts. Fever and staphylococcal skin infections occurred and were treated with antibiotics. After 10 days in clinically precarious condition, the patient began to regain granulocytes in the blood and his hematologic condition returned toward normal. This case illustrates the possibility of toxic suppression of bone marrow for several weeks following initiation of treatment or after change to a new agent in psychotropic drugs. The current incidence of agranulocytosis or serious leukopenia during treatment with psychotropic agents is not clear, but is believed to be unusual. 5 references.

001771 Dugas, James E. University of Connecticut, Storrs, **CT Mood elevation and medication.** Diseases of the Nervous System. 38(11):958, 1977.

The possibility of misuse, abuse or dependence on the antiextrapyramidal symptom agents trihexyphenidyl HCl (trihex) and benztropine mesylate (benz) is cautioned. As a result of numerous observations and subjective reports from both hospitalized and ambulant patients, it seems likely that trihex might possess a mild stimulant/euphoriant effect while benz seems to exert a mild sedating effect. The tremendous resistance to lowering of the dose or discontinuance of these medications from patients who had shown no extrapyramidal signs for many months is cited. 1 reference.

001772 Ende, Wolfgang; Hentschel, Frank. Nervenklinik Hochweitzschen, DDR-7301 Westewitz-Hochweitzschen, Germany **/Particularities of lithium intoxication in advanced age./ Zu einigen Besonderheiten der Lithiumintoxikation im hoheren Lebensalter.** Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 29(3):187-191, 1977.

Acute lithium intoxication in two gerontopsychiatric patients is described. Two females, aged 73 and 68, were readmitted for hospital treatment because of monophasic mania after poorly enforced lithium maintenance therapy at home. Each was placed on lithium and achieved remission within 2 days. An organic psychosyndrome developed without warning; vigilance was severely impaired and general health deteriorated. Fasting serum lithium levels were 1.25mval/1 and 2.6mval/1, respectively. Serum levels increased despite reduced lithium intake. Due to the patients' poor condition, neither dialysis nor sodium chloride infusion were attempted. Instead, manitol and antibiotics were administered, and the electrolyte/water metabolism was balanced. Despite high caloric intake, general health remained below norm for 6 to 8 weeks. Both patients showed abnormal EEG during the crisis. It is suggested that subclinical cardiovascular insufficiency may have contributed to poor cerebral circulation, possibly complicated by unidentified accessory influences. 18 references.

001773 Etsuno, Yoshifumi. Department of Neuropsychiatry, Kanazawa University, Kanazawa, Japan **EEG observation of nocturnal delirium in a patient taking antidepressants and antiparkinson's drugs.** Psychiatria et Neurologia Japonica (Tokyo). 79(3):166, 1977.

At the 74th Northern Japan Symposium for Neuropsychiatrists held in July, 1976 at the Kanazawa University Medical School, Japan, an EEG study of a 52-year-old man with manic-depression, who experienced nocturnal delusions while taking daily doses of 60 and 7.5mg of imipramine and methixene. His hands trembled so much that he was unable to write, while taking just the imipramine, so the methixene dosage was added. From the second day he had trouble sleeping, and his bodily movements and sleeptalking increased. From the 4th day of the combined dosage, there was delirium at night marked by hallucinations, audible hallucinations, and writhing around in bed. The delirium disappeared within 5 days when the methixene was discontinued. Four months before the delirium, EEG showed 11 to 12 second rhythms, with a lot of fast waves, but within normal limits. One week before the delirium, they showed 9 to 10 second alpha rhythms with a low-amplitude 6 to 7 sec activity. During delirium, slow waves were not prominent, with the alpha rhythm at 9 to 11 second rhythms. The fast wave component was small, and there was insufficient alpha attenuation while the eyes were open. It was concluded that many consciousness impairing side-effects

were noted in the middle-aged when antidepressants were combined with antiparkinson's drugs.

001774 Foerster, K.; Regli, F. Nervenklinik der Universitat, Osianderstrasse 22, D-7400 Tubingen, Germany /**Lithium therapy of extrapyramidal movement disorders.**/ Therapieversuch mit Lithium bei extrapyramidal-motorischen Storungen. Nervenarzt (Berlin). 48(4):228-232, 1977.

Lithium therapy of extrapyramidal movement disorders is reported. Patients (N=20) suffering extrapyramidal/motoric syndromes (excluding Parkinsonism) were treated with lithium sulfate or lithium carbonate in dosages that produced desirable blood sera levels. Significant improvement of motor disturbances was attained in three of the eight patients with Huntington's chorea, and this improvement was realized only if treatment was initiated in early stages of the disease. Improvement also occurred in three of four patients with tardive dyskinesia and in one of two patients with torticollis spasticus. A questionable improvement occurred in a patient suffering from Huntington's chorea, perioral dyskinesia in arteriosclerosis, and hemiballismus in encephalomalacia. No improvement was observed in two patients with torsidystonic syndromes or in one patient with choreoathetoid syndrome following pernicterus. 31 references. (Journal abstract modified)

001775 Friedman, Matthew J.; Culver, Charles M.; Ferrell, Richard B. Veterans Administration Hospital, White River Junction, VT 05001 **On the safety of long-term treatment with lithium.** American Journal of Psychiatry. 134(10):1123-1126, 1977.

Thirteen patients with bipolar affective illness who had received lithium therapy for 1 to 5 years were tested retrospectively for evidence of cortical dysfunction. Data on patients younger than 55 show no abnormalities on the Halstead-Reitan Neuropsychological Battery and suggest that chronic lithium therapy is relatively safe. Significantly elevated Halstead Impairment indexes were observed among elderly patients, but these data are difficult to interpret. 23 references. (Author abstract)

001776 Fuller, Colin M.; Yassinger, Sidney; Donlon, Patrick; Imperato, Thomas J.; Ruebner, Boris. Department of Internal Medicine, Section of Gastroenterology, University of California School of Medicine, Davis, CA 95616 **Haloperidol-induced liver disease.** Western Journal of Medicine. 127(6):515-518, 1977.

The cases of two schizophrenic patients in whom liver dysfunction developed during therapy with haloperidol are described. The dosages used were within the range recommended for severely disturbed psychiatric patients. In one patient a generalized hypersensitivity reaction developed; the other patient presented with painless jaundice. Biochemically, both patients showed evidence of mild hepatocellular disease and cholestasis. In neither patient was evidence of extrahepatic biliary obstruction found. Liver biopsy in the first patient showed evidence of a hypersensitivity reaction, with some hepatocellular necrosis, but predominant cholestasis. In the second patient, only cholestasis was seen. Haloperidol is felt to be etiologically related to the liver disease seen in these two patients. 14 references. (Author abstract)

001777 Gardos, George; Cole, Jonathan O.; La Brie, Richard A. Institute of Research and Rehabilitation, Boston State Hospital, 591 Morton Street, Boston, MA 02124 **Drug variables in the etiology of tardive dyskinesia application of discriminant function analysis.** Progress in Neuro-Psychopharmacology (Oxford). 1(1/2):147-154, 1977.

A stepwise discriminant function analysis was used to correlate etiological factors contributing to the development of tardive dyskinesia. Information was obtained from the medical records of 50 chronic, hospitalized, psychotic patients on numerous drug and nondrug variables. On the basis of the Simpson Tardive Dyskinesia Rating Scale, the study sample was dichotomized into dyskinesia and no dyskinesia groups. Analysis showed the following variables to discriminate significantly between the two groups: 1) duration of low potency neuroleptic; 2) previous EST; 3) length of neuroleptic therapy; 4) total amount of long-acting fluphenazine; and 5) abnormal EEG. The equation correctly classified 85.2% of no dyskinesia and 60.9% of dyskinesia patients. It is concluded that the discriminant function analysis is a useful tool in disentangling the relative importance of overlapping etiological factors in tardive dyskinesia. 15 references. (Author abstract modified)

001778 Goldfrank, Lewis; Osborn, Harold. Albert Einstein College of Medicine, New York, NY **The barbiturate overdose.** Hospital Physician. 13(9):30-34, 1977.

Barbiturate overdoses, their treatment, the scope of the problem, and possible preventive measures are discussed. Aggressive life support is identified as the current therapy for barbiturate overdose. Barbiturate poisoning is a major public health problem comprising 70% of all suicides by drug ingestion. Groups with a high incidence of suicide are reviewed and suggestions are made for the control of barbiturates. 11 references.

001779 Gottlieb, Jerome I.; Lustberg, Thomas. 8316 Arlington Blvd., Suite 516, Fairfax, VA 22030 **Phenothiazine-induced priapism: a case report.** American Journal of Psychiatry. 134(12):1445-1446, 1977.

A case report which supports the concept of priapism, the persistent abnormal erection of the penis without sexual desire, as a complication of phenothiazine therapy, is reported relevant to current theories of the physiology of male sexual activity. It is noted that in the present case, the ingestion of 1g of mesoridazine was related temporally to the development of priapism. 7 references.

001780 Greenberg, G.; Inman, W. H. W.; Weatherall, J. A. C.; Adelstein, A. M.; Haskey, J. C. Medicines Division, Department of Health and Social Security, London, EC2A 1PP, England **Maternal drug histories and congenital abnormalities.** British Journal of Medicine (London). No. 6091:853-856, 1977.

To examine possible associations between maternal drug history of benzodiazepine, barbiturate, antibiotic, and Hormonal Pregnancy Test use and congenital abnormalities in the child, drug histories were obtained for the first trimester of pregnancy for 836 mothers of congenitally malformed babies and for an equal number of control mothers of normal babies from the same doctors' practices. There was an association between the use of a hormonal pregnancy test and the subsequent birth of a malformed baby. There was also a greater use of barbiturates by mothers of affected children compared with mothers of control babies, mainly accounted for by treatment of epileptic mothers with phenobarbitone. For all other drugs usage was similar in both sets of mothers. 14 references. (Author abstract modified)

001781 Greenblatt, David J.; DiMascio, Alberto; Harmatz, Jerold S.; Bernardo, Diosdado L.; Marder, Joseph E. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA **Pharmacokinetics and clinical effects of amantadine in drug-induced extrapyramidal symptoms.** Journal of Clinical Pharmacology. 17(11&12):704-708, 1977

Plasma amantadine concentrations were assessed in a series of hospitalized schizophrenic patients receiving this drug during a double blind trial of amantadine and benztropine in the treatment of neuroleptic induced extrapyramidal symptoms (EPS). Mean plasma amantadine concentrations were 0.54 microgram/ml on day 7 and 0.43 microgram/ml on day 14. Overall improvement of EPS was not correlated with plasma level, but improvement in the target EPS of rigidity was correlated with plasma amantadine concentration on day 7 and day 14. There was no evidence that the overall improvement in schizophrenic symptomatology was influenced by plasma amantadine concentrations. 18 references. (Author abstract)

001782 Hall, Richard C. W.; Strong, Paul L; Popkin, Michael K.; Stickney, Sondra K. Clinical Research Unit, Texas Research Institute of Mental Sciences, 1300 Moursund Ave., Houston TX 77030 **Psychosis induced by Datura suaveolens: hallucinosis and anticholinergic delirium.** World Journal of Psychosynthesis. 9(3):19-22, 1977.

Hallucinosis and anticholinergic delirium in psychosis induced by Datura suavelons (Angel's Trumpet) is discussed, based on signs and symptoms seen in 31 cases of Datura poisoning. The clinical picture alternates between toxic delirium and an apparent functional psychosis manifested by agitation, auditory and visual hallucinations, impusivity, paranoia and loosening of associations. Over time the picture of toxic delirium becomes more stable. Visual hallucinations are similar to those reported ater LSD ingestion. Psychotic reaction and delirium are attributed to the alkaloids scopolamine, atropine, and hyoscyamine. Diagnostic guidelines are offered; gastric lavage and immediate i.v. administration of 1 to 4mg physostigmine is considered the treatment of choice. 8 references.

001783 Hamafuku, Shigeru; Uchida, Matako; Nishikawa, Masashi; Nishikawa, Mariko. no address **Four cases of syndrome Malin.** Psychiatria et Neurologia Japonica (Tokyo). 79(4):215, 1977.

At the 24th San'in District Symposium for Neuropsychiatrists, December 1976, Tottori, Japan, comparisons were made among four schizophrenics (three males) diagnosed as having syndrome malin. Two of the patients recovered and two died. All of the cases of syndrome malin showed excitedness, refusal to eat, tremors, sweating and drooling. They would then break out in a fever and show various autonomous nervous abnormalities. In two cases there was a rise in white blood corpuscles, GOT, and GPT, while in one there was a rise in CPK, LDH, and C1 levels. One case began after a large dosage of propericiazine and one after haloperidol. The other two cases had been taking normal dosages. Considerations on the prognosis of syndrome malin were made with regard to how soon psychotropic drug administration was stopped and the physical condition of the patient.

001784 Hartmann, Ernest. Sleep and Dream Laboratory, Boston State Hospital, Boston, MA **L-Tryptophane: an effective hypnotic.** Current Psychiatric Therapies. 17:165-169, 1977.

The use of l-tryptophane as an effective hypnotic in treating insomnia is compared with the use of CNS depressant hypnotics. It is noted that CNS depressants have the following underlying problems as a remedy for insomnia: 1) overdosing can cause death; 2) they are addictive; 3) tolerance develops rapidly; 4) they have a long half-life in the body, and produce hangover effects; 5) they react adversively in combination with some other medications; and 6) they produce a state which is not normal sleep by polygraphic criteria. L-Tryptophane is suggested as a hypnotic medication of choice for insomnia as it is effective in producing a reduction in sleep latency and in waking time and is a FDA GRAS (generally recognized as safe) food substance. 17 references.

001785 Hegarty, J. E.; Dundee, J. W. Dept. of Anesthetics, Queen's University of Belfast, Belfast, Northern Ireland **Sequelae after the intravenous injection of three benzodiazepines -- diazepam, lorazepam, and flunitrazepam.** British Medical Journal (London). No. 6099:1384-1385, 1977.

The occurrence of thrombosis and phlebitis after intravenous injection of 10mg diazepam, 4mg lorazepam, or 1 to 2mg flunitrazepam was studied on the second or third and the seventh to 10th days. A significantly higher incidence occurred with all drugs on days 7 to 10 than on days 2 and 3. Painless thrombosis occurred much more often with diazepam than with the other two benzodiazepines. Its incidence was greater in small hand or arm veins than in large antecubital vessels. It is concluded that venous thrombosis is a not infrequent consequence of the intravenous injection of undiluted benzodiazepines, and that lorazepam and flunitrazepam show clear advantages over diazepam in this respect. 5 references. (Author abstract)

001786 Herskowitz, Joel; Oppenheimer, Edgar Y. Boston City Hospital, Boston, MA 02118 **More about poisoning by phencyclidine ("PCP," "angel dust** New England Journal of Medicine. 297(25):1405, 1977.

To call attention to eye movement abnormality as a useful clinical sign for diagnosis of phencyclidine (angel dust, PCP) poisoning, two cases of PCP toxicity in adolescent males are reported in a letter to the editor. Both patients presented with obtundation, blunted reaction to painful stimuli, ataxia, and mutism. In addition, striking bursts of irregular, shuddery, jerk nystagmus occurred in the direction of horizontal and vertical gaze, with the greatest amplitude being seen for upward gaze. Although mental status improved within 24 hr, nystagmus continued through the fourth day following admission. Recognition of this abnormality of eye movement may aid in an earlier and more definitive diagnosis of PCP poisoning. 5 references.

001787 Hindmarch, Ian. Dept. of Psychology, University of Leeds, Leeds LS2 9JT, England **A repeated dose comparison of three benzodiazepine derivatives (nitrazepam, flurazepam and flunitrazepam) on subjective appraisals of sleep and measures of psychomotor performance the morning following night-time medication.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(5):373-381, 1977.

To examine the effects of three benzodiazepine derivatives on subjective appraisals of sleep and on psychomotor and cognitive performance the morning following night time medication, 30 healthy volunteers received repeated doses of nitrazepam, flurazepam, or flunitrazepam in a 10 day double-blind study. Repeated doses of 5mg nitrazepam, 15mg flurazepam, and 1mg flunitrazepam improved subjective assessments of the ease of getting to sleep and the perceived quality of induced sleep. The subjective reports of improved sleep inducement were related to a perceived difficulty in awakening from sleep the morning following medication. This subjectively reported hangover is also shown in the impairment of mental arithmetic abilities as measured on the serial subtraction of sevens technique. However, complex psychomotor performance is unaffected by repeated administration of these three benzodiazepine derivatives, although these later results are somewhat equivocal. Evidence of a rebound phenomenon following 4 nights' withdrawal of active medication is shown

on both subjective and objective measures of sleep and early morning behavior. 23 references. (Author abstract modified)

001788 Hudson, Page; Barringer, Michael; McBay, Arthur J. Office of the Chief Medical Examiner, PO Box 2488, Chapel Hill, NC 27514 **Fatal poisoning with propoxyphene: report from 100 consecutive cases.** Southern Medical Journal. 70(8):938-942, 1977.

One hundred deaths attributed to propoxyphene, a centrally acting narcotic analgesic usually sold as Darvon, were studied by the Chief Medical Examiner of the state of North Carolina. Victims ranged evenly in age from the second to the seventh decade. Over 65% were suicides with a female to male ratio of 2:1. Blood propoxyphene concentrations of 0.2mg/dl were fatal, representing rapid ingestion of approximately ten capsules. In North Carolina, deaths due to propoxyphene have increased from five in 1969 to 49 in 1975. Raising physician awareness of propoxyphene's toxicity and placing the drug in Schedule II are two recommendations for reducing the number of propoxyphene deaths. 19 references. (Author abstract modified)

001789 Iivanainen, M.; Viukari, M.; Helle, E.-P. Dept. of Neurology, University of Helsinki, Helsinki, Finland **Cerebellar atrophy in phenytoin-treated mentally retarded epileptics.** Epilepsia. 18(3):375-386, 1977.

The relationship among the serum concentration of phenytoin, pneumoencephalographic measurements describing cerebellar atrophy, and various other clinical variables was analyzed statistically in a series of 131 phenytoin treated mentally retarded epileptics. Results show that phenytoin levels in serum correlated significantly with the heights of the fourth ventricle suggests that an overdosage of phenytoin or an underlying disease, or both, were the probable causes of cerebellar impairment and atrophy. Brain-damaged mentally retarded epileptics appear to be unusually susceptible to the side-effects of phenytoin. 38 references.

001790 Innes, J. A.; Watson, M. L.; Ford, M. J.; Munro, J. F.; Stoddart, Margaret E.; Campbell, D. B. Eastern General Hospital, Edinburgh, Scotland **Plasma fenfluramine levels, weight loss, and side effects.** British Medical Journal (London). No. 6098:1322-1325, 1977.

The correlation between fenfluramine dosage, weight loss, and side-effects with plasma fenfluramine and norfenfluramine concentrations in 50 women with refractory obesity was investigated in a 20 week study. Every 2 weeks details of weight change, drug dose, degree of anorexia, and any side-effects were recorded and plasma was obtained for fenfluramine and norfenfluramine. Of the 41 patients available for final analysis 26 achieved a maximum plateau dose of 160mg/day. Plasma fenfluramine concentrations did not correlate with the degree of anorexia or with the incidence of side-effects other than the severity of dream disturbance. There was a highly significant relation between weight loss and plasma fenfluramine and norfenfluramine concentrations and also between weight loss and the presence of sustained anorexia. It is concluded that when fenfluramine is prescribed in refractory obesity the dose should be increased stepwise until either satisfactory weight loss is achieved or troublesome side-effects appear. 29 references. (Author abstract modified)

001791 Jansen, F. H. J.; Drykoningen, G.; de Ridder, J. J. Organon Scientific Development Group, Organon International BV, Oss, The Netherlands **Poisoning with antidepressants.** British Medical Journal (London). No. 6091:896, 1977.

In a letter to the editor, a case of attempted suicide in a 53-year-old woman is reported to elucidate antidepressant toxic effects. The patient consumed over 600mg mianserin in combination with sleeping tablets and alcohol. Upon admission the patient was in a deep coma. Repeated electrocardiograms showed no abnormalities apart from left axis deviation. Hemodialysis was performed for 6 hours in an attempt to lower plasma mianserin levels. However, pharmacokinetic analysis of mianserin concentrations indicated first-order kinetics which were influenced by hemodialysis. The patient awoke 17 hours after ingestion and recovery was uneventful. It is concluded that hemodialysis is not effective in the management of mianserin overdose, and that mianserin overdosage does not produce cardiotoxicity.

001792 Johnston, Brian B. Royal Dundee Liff Hospital, Dundee DD2 5NF, Scotland **Diabetes mellitus in patients on lithium.** Lancet (London). No. 8044:935-936, 1977.

Two cases are reported in which a possible association between lithium therapy for depressive psychosis and onset of diabetes mellitus is suggested. In both cases subjects diagnosed as depressive psychotics eventually died after lithium therapy with indications of diabetes mellitus. Reference is made to two other cases reported elsewhere in which lithium therapy is associated with diabetes. It is suggested that thirst, polyuria, and fatigue in a patient on lithium should not be dismissed as common, and therefore acceptable, side-effects of the treatment. 4 references.

001793 Kobayashi, Shigeru; Hirada, Junichiro; Hisazato, Toshiaki; Yamamoto, Kenji; Honda, Noriyuki; Ueno, Nobuya, Shinagawa, Shoji. no address **On cataracts seen during psychotropic drug therapy.** Psychiatria et Neurologia Japonica (Tokyo). 79(4):206-207, 1977.

At the 26th Central Japan Shikoku Symposium of Neuropsychiatrists, November 1976, Okayama, Japan, a case of probable psychotropic drug caused cataracts in a 44-year-old man is reported. The man had been taking butyrophenonetype drugs, and his cataracts were treated successfully with surgery. This same type of drug has also been known to cause eye problems in other patients. In two other patients, a crystalline type of turbidity was found on the cornea. Because these patients were on many drugs, it was impossible to establish cause and effect relationships. These results were discussed in relation to other reports of psychotropic drug related eye problems.

001794 Koizumi, Shinsuke; Takatani, Yuzo; Kumashiro, Hisashi. Department of Psychiatry, Fukushima Red Cross Hospital, Fukushima, Japan **On the course of methamphetamine (Philopon) psychosis.** Psychiatria et Neurologia Japonica (Tokyo). 79(7):368, 1977.

Seven cases of philopon (phenyl methyl aminopropane) intoxication and their symptoms were examined in a study presented at the 31st Symposium for Northeastern Japanese Neuropsychiatrists held in October 1976 at the Miyagi Prefectural Doctor's Hall. Symptoms of philopon intoxication are consciousness impairing and resemble those of schizophrenia or manic-depression. One of the subjects had been placed in solitary confinement for 11 months and was still showing diverse schizophrenic symptoms. All had aftereffects and symptoms from their amphetamine intoxication. The similarities and disparities between philopon intoxication and schizophrenia were discussed.

001795 Konigshausen, Th.; Hein, D.; Grabensee, B. I. Med. Klinik A, Universitat Dusseldorf, Dusseldorf, Germany **The human EEG in severely poisoned patients -- indication and control of hemodialysis or hemoperfusion.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):71-77, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, the use of EEG's as an indicator of the degree of severity of a drug intoxication due to hypnotics and barbiturates, and of the control of the patient through hemodialysis or hemoperfusion, is described. Seventy-three patients with severe hypnotic intoxication due to the following agents were evaluated: barbiturate (n=20), carbromal (n=24), mixed (n=19), benzodiazepine (n=4), amitryptiline (n=2), metaqualon (n=2), metyprylone (n=1), and gluthetimide (n=1). The use of the EEG in hypnotic overdosage management is encouraged for the following reasons: 1) the cases evaluated indicated the EEG to be a sensitive parameter for clinical interpretation of the severity of the intoxication, more rapidly acquired than serum level indicators; 2) intermittant silent periods or initial isoelectric patterns provide an indication for immediate use of hemodialysis or hemoperfusion; and 3) the EEG provides a tool for controlling the need for continued usage of hemodialysis or hemoperfusion. It is noted that persistent isoelectric patterns is suspect of irreversible encephalomalacia due to cerebral hypoxia. 12 references.

001796 Kubo, Setsuji; Kodama, Hidetoshi; Sueda, Kaku; Kamada, Toru. Kamo-Byoin National Sanatorium, Hiroshima, Japan **Sudden death of patients using psychotropic medication.** Iryo (Tokyo). 31(7):57-61, 1977.

Two autopsy cases of patients who died of bleeding of the lung after taking psychotropic medication are reported, along with two other nonfatal cases who suffered bleeding of the lung. The bleeding was suspected to have been caused by a pulmonary embolism on the macroscopic findings, but there was no congestion or bleeding of the other organs. Dosages had been 15mg of haloperidol and 6mg of reserpine daily for one patient, but there was no common type of psychotropic drug nor dosage which correlated with the lung bleeding. In the other two cases, they collapsed, became feverish, and were diagnosed and treated for pulmonary suppuration. While no concrete relationship between the bleeding of the lung and the psychotropic medication could be found, further research on a possible link is suggested. 15 references. (Author abstract modified)

001797 Kudsk, Folmer Nielsen; Schou, Mogens. Aarhus University Institute of Pharmacology, Aarhus, Denmark **Mercury content of medicinal lithium preparations.** Journal of Pharmacy and Pharmacology (London). 29(12):776-777, 1977.

To determine mercury content of medicinal lithium preparations used in the treatment of manic-depressive disorder, 23 lithium preparations from 14 countries were analyzed. The preparations fell into three groups: 1) content close to or below the detection limit -- 17 preparations; 2) 20ng to 40ng mercury per tablet -- three preparations; and 3) one preparation containing 1450ng per tablet and a lithium carbonate powder containing 40ng per 50mg. Mercury in preparations containing the highest concentrations was inorganic. Given the average lithium dosage, mercury intakes for all three classes are well below the provisional tolerable weekly intake of mercury. It is concluded that amount of mercury administered with lithium tablets is probably without toxicological significance. 5 references.

001798 Kusumo, K. S.; Vaughan, M. Department of Clinical Psychology, Faculty of Psychology, University of Indonesia, Jl Salemba No. 4, Jakarta, Indonesia **Effects of lithium salts on memory.** British Journal of Psychiatry (London). 131:453-457, 1977.

To examine possible effects of lithium therapy on memory functions, 13 patients diagnosed as having affective disorders, and who were taking lithium, were compared with drug free controls on short-term and long-term memory tasks. There was some indication that patients on lithium may show an impairment of short-term memory at 15 second delay intervals, and possibly enhanced long-term recall of difficult material. Further comparison with results obtained from six patients on tricyclic antidepressants seemed to reduce the possibility that the lithium group's scores were a function of their psychiatric status. As the group sizes were small, all the findings need to be replicated. 8 references. (Author abstract modified)

001799 Lal, Kasturi; Jammihai, J. H. Department of Obstetrics and Gynecology, Medical College, Jammu, Kashmir, India **Phenobarbitone teratogenicity: a case report.** Clinician (Panjim-Goa). 41(7):274-277, 1977.

A case report of phenobarbitone teratogenicity is reported, in which an infant born to a mother who had received barbiturates throughout pregnancy, demonstrated the primary microcephaly and other skeletal deformities. It is concluded that phenobarbitone has teratogenic action, although such action is likely to be influenced by hereditary and environmental factors. The infant had mild convulsions which were treated with oral glucose and phenobarbitone successfully. 11 references. (Author abstract modified)

001800 Leber, H. W.; Geissler, R. H.; Post, D. University Hospital, Giessen, Germany **Carbromal intoxication -- hemodialysis or hemoperfusion?** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):78-84, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, experiments conducted to determine whether hemoperfusion (through charcoal or Amberlite) or hemodialysis is most effective in eliminating carbromal intoxication are reported. Carbromal, a frequently used drug for self-poisoning, is said to evoke toxic effects in the lungs, heart and hemostatic system, and bears a high risk of lethality. Measurements of in vitro and in vivo clearances of carbromal plasma concentrations and all the metabolites containing the ureide structure were taken. Amberlite perfusion was shown to be the most effective means to remove carbromal and its active metabolites from body fluids. However, it is noted that hemodialysis should be preferred to hemoperfusion when coagulopathies exist, since a known side-effect of hemoperfusion is thrombocytopenia. 16 references.

001801 Leiber, Lillian. Department of Neurology, Edward J. Meyer Memorial Hospital, Buffalo, NY 14215 **Psychological side-effects of L-dopa and anticonvulsant medication.** New York State Journal of Medicine. 77(7):1098-1102, 1977.

In a paper presented at a symposium on Iatrogenic Disorders of the Nervous System held at the State University of New York at Buffalo, literature is reviewed which indicates that adverse effects on psychological functioning occur in approximately 20% of parkinsonian patients receiving L-dopa and in 20% of epileptic patients receiving anticonvulsant medications. Psychiatric disturbances occur more frequently in patients with postencephalitic parkinsonism, in patients who are

elderly and/or demented, or who have a poor premorbid psychiatric history. The intellectual and psychiatric disturbances associated with anticonvulsant medications are more closely related to serum anticonvulsant levels than to dosage. It is suggested that the very young, the very old, and the severely disabled require particularly careful monitoring because signs of toxicity may be masked. 49 references.

001802 Lianantonakis, E. Second Psychiatric Clinic, Athens State Mental Hospital, Athens, Greece **Obesity related to the use of psychotropic drugs, considered in its psychodynamic aspect.** Behavioral Neuropsychiatry. 8(1-12):73-75, 1977.

The psychodynamic aspect involved in obesity related to the use of psychotropic drugs is examined. This type of obesity is labeled psychopharmacotherapeutic obesity and is discussed from the standpoint of etiogenesis, psychological effects, and its importance in relation and conjunction with the development and formation of the individual's psychosomatic identity. It is regarded as a serious side-effect because obesity is often the main reason why the patient discontinues his psychopharmaceutical therapy, and thus causes a recurrence of his mental illness. 7 references.

001803 Lianantonakis, E.; Kotroutsos, E.; Zacharakopoulou, E. Second Psychiatric Clinic, Athens State Mental Hospital, Athens, Greece **Obesity related to the use of psychotropic drugs, considered in its organic aspect.** Behavioral Neuropsychiatry. 8(1-12):36-38, 1977.

The organic aspects of obesity as related to the use of psychotropic drugs are discussed. The diagnostic term psychopharmacotherapeutic obesity is applied to this type of obesity and its probable etiopathogenetic mechanism is examined. It is suggested that endocrinal dysfunctional disturbances in the hypothalamic origin caused by psychotropic drugs results in increased body weight. It is concluded that this side-effect is serious because many patients discontinue their psychotropic drug treatment due to obesity, and thus suffer a mental relapse. 28 references.

001804 Lieb, Julian. Dana Psychiatric Clinic, Yale-New Haven Hospital, 789 Howard Ave., New Haven, CT 06504 **Degraded protein-containing food and monoamine oxidase inhibitors.** American Journal of Psychiatry. 134(12):1444-1445, 1977.

Three case reports of patients with hypertensive reactions to degraded protein containing food are reported, in which the offending agent appears to have been denatured protein rather than the specific items that usually appear on the diet lists of patients on monoamine oxidase inhibitors (MAOIs). It is noted that the four reactions reported, including severe headache and elevated blood pressure, lend support to the conclusion that the foods that have been reported to cause hypertensive reactions may have in common the degradation of a protein constituent, and that only fresh food or freshly prepared frozen or canned food should be eaten by patients on MAOIs. 6 references.

001805 Lindstedt, Goran; Nilsson, Lars-Ake; Walinder, Jan; Skott, Annika; Ohman, Rolf. Dept. of Clinical Chemistry, Sahlgren's Hospital, S-41345 Goteborg, Sweden **On the prevalence, diagnosis and management of lithium-induced hypothyroidism in psychiatric patients.** British Journal of Psychiatry (London). 130:452-458, 1977.

The prevalence, diagnosis, and management of lithium induced hypothyroidism was studied in a group of 53 psychiatric patients on lithium therapy for 2 years, a hypothyroid group of 24 patients, and a control group of female psychiatric patients. The study showed that in the lithium group the males were not affected while 20% of the 39 women were. In the hypothyroid group the average duration of lithium treatment before the appearance of hypothyreosis was 2 years and 10 months. In 8 of the patients the symptoms, weight gain and fatigue, appeared within the first year, and three experienced symptoms within the first 6 months. All cases of lithium induced hypothyroidism showed elevated levels of serum thyrotropin, a well known indicator of primary hypothyroidism. It is noted that hypothyroid patients responding well to lithium should continue their medication combined with appropriate thyroxine substitution. 19 references.

001806 Malizia, E.; Signore, L.; Crimi, G. Istituto Anesthesiologia e Rianimazione Universita di Roma, Roma, Italia **Chlorpromazine plus thioridazine poisoning and treatment with extracorporeal dialysis.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):163-170, 1977.

In a paper presented at the 7th International Congress of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, a case is reported of the treatment of chlorpromazine and thioridazine poisoning via extracorporeal dialysis. Forty eight hours after hospitalization, the patient relapsed into deep coma with respiratory insufficiency, and extracorporeal dialysis through a Travenol Coil kidney was initiated. Following 6 hours of treatment, the patient was completely conscious and needed no intensive care. The coma, uremia, and possible kidney damage following overdoses of chlorpromazine and thioridazine are discussed. 42 references.

001807 Marttila, James K.; Hammel, Richard J.; Alexander, Bruce; Zustiak, Robert. College of Pharmacy, University of Minnesota, Minneapolis, MN **Potential untoward effects of long-term use of flurazepam in geriatric patients.** Journal of the American Pharmaceutical Association. 17(11):692-695, 1977.

A study in five skilled nursing facilities and two intermediate care facilities was conducted to identify the frequency and severity of untoward effects associated with the long-term use of flurazepam in geriatric patients. Of 750 patients, 195 had received the drug during the previous year. Twenty six percent of these 195 patients had experienced problems such as ataxia, confusion and hallucinations. Patients receiving flurazepam who experienced untoward effects generally fell into two groups: one group had received the drug twice a week or less, and the other group received the drug at least five times a week. As a result of the documentation of the problem by consultant pharmacists, the chronic use of flurazepam and other hypnotic agents was sharply reduced in the long-term care facilities. 20 references. (Author abstract)

001808 Mehta, D.; Mehta, S.; Mathew, P. Geriatrics Program, Missouri Institute of Psychiatry, 5400 Arsenal, St. Louis, MO 63139 **Tardive dyskinesia in psychogeriatric patients: a five-year follow-up.** Journal of the American Geriatrics Society. 25(12):545-547, 1977.

The status of tardive dyskinesia in 13 elderly patients at the 5 year followup point is discussed with regard to increasing concern for the neurological side-effects of antipsychotic drugs. In 11 of the 13, tardive dyskinesia persisted. Among these 11 patients, the severity was reduced in 2, increased in 2, and unchanged in 7. Only in 2 of the total 13 subjects had the tardive dyskinesia disappeared. However, both of these patients were receiving neuroleptic drugs and had parkinsonism, a syndrome that might have masked the dyskinesia.

Recommendations are made for prophylaxis and for good clinical judgment in the use of antipsychotic drugs. 10 references. (Author abstract)

001809 Meisler, Arnold I.; Stein, Richard S. University of Rochester Medical Center, Rochester, NY 14642 **Lithium carbonate in chemotherapy-induced neutropenia.** New England Journal of Medicine. 297(21):1179-1180, 1977.

In a letter to the editor, the possible effects of lithium carbonate in chemotherapy induced neutropenia are discussed. It is hypothesized that if the proliferating function of cells in the marrow exceeds that in the tumor, severe toxicity will eventually supervene. If lithium carbonate actually causes the mobilization of granulocyte precursors from a resting to a growing state, the long-term consequences may, it is argued, be dire. Although initially decreased leukopenia may be observed, successive cycles of therapy including lithium carbonate should result in profound and rapid bone marrow depletion. A cardinal rule is suggested for the chemotherapist, which is to avoid administration of cytotoxic drugs during periods of intense marrow activity such as results from infection, recovery from previous chemotherapy or even during acute immunostimulation.

001810 Menzies-Gow, Neil; Nelson, Peter G. Central Middlesex Hospital, London NW10, England **Cimetidine and mental confusion.** Lancet (London). No. 8044:928, 1977.

Two incidences of mental confusion associated with the administration of cimetidine, an H2 receptor blocking agent, are reported. In the first case a normal dose of cimetidine was followed by drowsiness, confusion, restlessness, and unmanageability, all of which disappeared after treatment was stopped. The second case involved an overdose that was treated with gastric lavage where a high pulse rate was noted along with agitation and disorientation. It is concluded that these and other reports add weight to the suspicion that cimetidine may occasionally cause cerebral toxicity. 5 references.

001811 Molnar, I.; Slaastad, R. M.; Loes, O.; Sund, A. no address **A case of conservatively managed lithium intoxication.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):180-187, 1977.

In a paper read at the 7th International Congress of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, a case report of the treatment of a suicidal 39-year-old male with acute lithium intoxication is presented. Neurological damage and sequelae have been major problems in the management of patients with lithium intoxication. Sedative and anticonvulsive medication, including curare, made assessment of neurological status during the acute phase uncertain. Three weeks after admission, the patient was cooperative, but had slow cerebration. He had amnesia for the period of acute illness, and difficulties with concentration and recent memory. Reported cases of lithium intoxication are reviewed briefly. 9 references.

001812 Monma, Yoshimichi; Takamatsu, Kozo; Kokasahara, Susumu; Kimura, Hidekazu. Department of Neuropsychiatry, Tohoku University, Tohoku, Japan **One autopsy case of diphenylhydantoin intoxication.** Psychiatria et Neurologia Japonica (Tokyo). 79(7):367, 1977.

At the 31st Symposium for Northeastern Japanese Neuropsychiatrists held in October 1976 at the Miyagi Prefectural Doctor's Hall, an autopsy case of a patient with diphenylhydantoin (DPH) intoxication was reported. The 30-year-old woman had external head injuries from accidents at the ages of 8 and 24 and was subject to seizures since she was nine. She began taking DPH at 24. Autopsy findings indicated that the cerebellum had shrunk and that cellular damage had occurred in that area. This along with other pathohistological examinations of the brain suggested that epilepsy was not the cause of the damage. No direct cause of death could be ascertained, but the brain damage was extensive enough to be suspected as the contributing cause.

001813 Nair, N. P. V. Douglas Hospital, 6875 La Salle Blvd., Montreal, Quebec H4H 1R3, Canada **Drug therapy of schizophrenias in the community.** Journal of Orthomolecular Psychiatry (Regina). 6(4):348-353, 1977.

The problems and prospects of maintenance drug therapy of schizophrenia in the community are discussed. Studies are reviewed which indicate that in the majority of chronic schizophrenic patients, maintenance medication may be unnecessary. This is thought to be especially true for those patients who are on a low dosage maintenance, and it is suggested that drug therapy may even inhibit the reintegration of these patients into the community. In addition these tranquilizers and neuroleptics are proven to cause negative side-effects such as Parkinsonism, akathisia, and dyskinesia. 29 references.

001814 Nevins, Donald B. Department of Psychiatry, University of California School of Medicine, San Francisco, CA **Adverse response to neuroleptics in schizophrenia.** International Journal of Psychoanalytic Psychotherapy. 6:227-241, 1977.

Negative therapeutic reactions to neuroleptics in schizophrenic patients are examined from the psychoanalytic perspective through case examples. Intrapsychic changes resulting from this medication, ordinarily considered beneficial, are shown, in some cases, to be disruptive of schizophrenic functioning and organization and potentially to endanger the continuation of medication itself. Changes are described which effect defenses, object relations, psychotic restitution, use of external reality, body image and cognition, and the symbolic significance of medication. Alterations in narcissistic ego states and disruption in preconscious processes, superimposed upon defective ego functioning, are used as explanatory concepts. These interact with transference based responses; in some cases, important psychodynamic issues emerge amenable to transference interpretations. Further study of intrapsychic changes may be useful in delineating a previously inexplicable response, understanding symptom formation, recognizing shifts in the patient-psychotherapist relationship, and forestalling premature cessation of medication. 33 references. (Author abstract)

001815 no author. no address /**Sleeplessness due to soporifics?**/ Schlaflosigkeit durch Schlafmittel? Praktische Psychiatrie (Zurich). 56(6):162, 1977.

Long-term effects of soporifics on sleep were investigated. Research conducted at the Hannover Medical School indicates that so called sleep inducing agents produce, largely through self-deception, a state which resembles sleep, but which in fact prevents normal phases of sleep. Withdrawal of such drugs triggers increased sleep disturbances, leading to the conclusion that every hypnotic dictates its own habituation, even when sleep is no longer induced. Since most nonprescription sedatives contain bromide salts or organic bromine compounds, habitual intake may lead to gradual bromine poisoning. Such a toxic condition is manifested initially by sleep disturbances, deceleration of cognition and activity, memory lapses, and depressive mood.

001816 no author. no address **Drug-induced depression.** Lancet (London). No. 8052/3:1333-1334, 1977.

Depression induced by various kinds of drugs is discussed. Depression has been reported as a side-effect of antihypertensives, corticosteroids, oral contraceptives, levodopa, indomethacin, fenfluramine, physostigmine choline, certain antibiotics, diazepam, digitalis, sulfonamides, metronidazole, and oral and depot phenothiazine and thioxanthene preparations. The depressive effect is attributed to interference with the metabolism of brain monoamine transmitters, particularly catecholamines, indoleamines and acetylcholine. The metabolic process is described and the ways some drugs exert their depressive effect by acting on a specific site is discussed. The role of drug induced depression in suicides is also considered. 26 references.

001817 Nora, Audrey H.; Nora, James J.; Blu, Janet. Dept. of Pediatrics, University of Colorado Medical Center, Denver, CO 80262 **Limb-reduction anomalies in infants born to disulfiram-treated alcoholic mothers.** Lancet (London). No. 8039:664, 1977.

In a letter to the editor, the possibility that disulfiram administered to pregnant mothers can produce significant birth defects is discussed in light of the knowledge that alcohol consumption, for which the disulfiram is administered, can also cause birth defects. A review of 1320 teratogenic histories revealed severe limb reduction anomalies in the only two mothers who had been maintained on a disulfiram sobriety regimen during pregnancy. The limited total experience of maldevelopment of limbs in several cases suggests that care should be taken with the use of disulfiram to combat alcoholism in women of reproductive age. 4 references.

001818 Nowlan, Robert; Cohen, Sidney. Neuropsychiatric Institute, University of California at Los Angeles Center for Health Sciences, Los Angeles, CA 90024 **Tolerance to marijuana: heart rate and subjective "high."** Clinical Pharmacology Therapeutics. 22(5):550-556, 1977.

Findings on the effects of ad lib marihuana smoking on heartrate and experienced high through a 94 day period are presented. In a 94 day supervised study of 30 subjects smoking marihuana, with drug free periods interspersed, mean heartrate and subjective high decreased over the smoking period. Light smokers had greater chronotropic and subjective effects than heavy smokers, but both demonstrated evidence of tolerance. Cumulation and minor withdrawal effects are noted. 13 references. (Author abstract modified)

001819 Oliver, John S.; Watson, Alan A. Dept. of Forensic Medicine, University of Glasgow, Glasgow, Scotland **Oxprenolol (Trasicor) poisoning.** Medicine, Science and the Law (Bristol). 17(4):279-281, 1977.

The details of a fatal case of oxprenolol poisoning in a physically healthy adult female are presented. Patient was suffering from chest pains and an apparently progressive depression. Overdose was an apparent suicide. The level of oxprenolol found in the liver was 5.8mg/100g, which indicates the amount of the drug likely to cause death. It is concluded that the supply and use of oxprenolol should be under careful supervision. 2 references.

001820 Pall, H.; Czech, K.; Kotzaurek, R.; Kleinberger, G.; Pichler, M. First Medical Clinic of Vienna, Intensive Care Unit, Vienna, Austria **Experiences with physostigminesalicylate in tricyclic antidepressant poisoning.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):171-178, 1977.

In a paper presented at the 7th International Congress of the European Association of Poison Control Centres, held at Oslo, Norway during June 1976, experiences with physostigmine salicylate administered to 15 patients with severe tricyclic antidepressant poisoning was discussed. After an initial bolus injection followed by a continuous intravenous administration of physostigmine, the sensorium of the comatose patients improved rapidly. In patients with serious cardiac arrhythmias the potent antiarrhythmic action of physostigmine was established. Physostigmine proved to be a safe and effective antidote to toxic effects of tricyclic antidepressants. The short half-life time of physostigmine implies a continuous intravenous administration over hours to avoid another deterioration of the sensorium or the cardiac rhythm. The exacerbation of a chronic alcoholic pancreatitis under the treatment with physostigmine is also discussed. 10 references. (Author abstract modified)

001821 Park, J.; Proudfoot, A. T. Royal Infirmary, Edinburgh, Scotland **A seven year review of coma patients admitted to the Regional Poisoning Treatment Centre, Royal Infirmary, Edinburgh.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):516, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, a 7 year review of poison induced coma patients who were admitted to the Regional Poison Treatment Center, Royal Infirmary in Edinburgh is presented. Age and sex distribution and management support of patients assessed to be in coma grades 2, 3, and 4 according to Matthew and Lawson criteria were reported. A changing pattern was demonstrated in the use of principle poisons. Although decreased in usage, barbiturates remained the most commonly encountered poisons causing grade 3 and 4 coma. The incidence of methaqualone poisoning decreased and tricyclic antidepressant overdosage increased. Treatment techniques and mortality statistics are discussed. (Journal abstract modified)

001822 Petit, James M.; Biggs, John T. Department of Psychiatry, Washington University School of Medicine, 4940 Audubon Avenue, St. Louis, MO 63110 **Tricyclic antidepressant overdoses in adolescent patients.** Pediatrics. 59(2):283-287, 1977.

Overdosage of tricyclic antidepressants is discussed with special reference to adolescents under 18 years of age. Of a total of 36 patients ingesting primarily tricyclic overdoses 16 were 18 to 30 years old, and 9 were 13 to 17 years old. In the younger group, six patients were female and three were male. Drugs ingested were amitriptyline, imipramine, desipramine, and doxepine, with eight of the nine patients taking only one drug. Seven of the nine patients ingested their own medications. Two patients had plasma levels over 1000ng/ml, which is considered medically serious. Four of the suicide attempts were considered psychiatrically serious. Of these four patients, two suffered from primary affective disorder and two were undiagnosed. The other five diagnoses were anxiety neurosis, antisocial personality, hysteria, primary affective disorder, and undiagnosed psychiatric illness. 16 references.

001823 Pollack, Michael A.; Cohen, Neal L.; Friedhoff, Arnold J. Epilepsy Research Center, Fondren 652A, Texas Medical Center, Houston, TX 77030 **Gilles de la Tourette's syndrome: familial occurrence and precipitation by methylphenidate therapy.** Archives of Neurology. 34(10):630-632, 1977.

The occurrence of Gilles de la Tourette's syndrome in two male cousins once removed, and its precipitation by methylphenidate therapy are reported. Previous studies have shown familial clustering of individuals with tics, but no consistent pattern of inheritance of Tourette's syndrome has been apparent. The onset and later exacerbation of symptoms in the younger patient were associated with the administration of CNS stimulants given for excessive motor activity. The adverse effects of methylphenidate and dextroamphetamine therapy on Tourette's syndrome supports the hypothesis that this condition results from a relative excess of CNS catecholaminergic activity. Physicians prescribing these agents should inquire about the presence of tics in patients and their families. 19 references. (Author abstract modified)

001824 Prescott, L. F. Royal Infirmary, Edinburgh, Scotland **Iatrogenic complications of drug overdosage and poisoning.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):64, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, the position is advanced that basic management of drug overdosage and poisoning should consist of intensive supportive therapy with a minimum of drug treatment such as saline emetics, pressor agents or physostigmine, due to their potential and sometimes fatal complications. Tricyclic poisoning is used as an example. It is pointed out that the use of cardiotoxic antiarrhythmic drugs for the treatment of usually transient arrhythmias seen in tricyclic intoxications is a dangerous and unnecessary treatment, and should be replaced by control of convulsions, acidosis and hypoxia to attain the therapeutic objective. (Author abstract modified)

001825 Rainey, John M., Jr. Wayne State University School of Medicine, Detroit, MI **Antabuse toxicity.** Current Psychiatric Therapies. 17:265-268, 1977.

Toxicity resulting from disulfiram (Antabuse) administration used in the treatment of alcoholism is described. A characterization of mild, moderate and severe toxic reactions is presented, along with dose response relationships associated with them. It is noted that Antabuse toxicity resembles known sequelae of severe alcoholism, e.g.,psychosis, delirium, peripheral neuropathy and hepatic damage, and that consequently, assessments of mental, neurological and hepatic status should precede initiating therapy in order to be able to assess possible toxic reaction. No detectable, permanent damage has been found from Antabuse side effects. Treatment of the toxic reaction is suggested as discontinuation of the drug and thiamine supplements. 4 references.

001826 Rogers, Howard J.; Haslam, Robert A.; Longstreth, James; Lietman, Paul S. Dept. of Pharmacology, Guy's Hospital Medical School, London SE1 9RT, England **Phenytoin intoxication during concurrent diazepam therapy.** Journal of Neurology, Neurosurgery, and Psychiatry. 40(9):890-895, 1977.

Phenytoin intoxication during concurrent diazepam therapy was investigated in two children, ages 3 and 6 years, under treatment for convulsions following brain damage. Intravenous phenytoin infusions were given and the apparent Km and Vmax were computed from the resulting plasma phenytoin levels. These were compared to phenytoin Km and Vmax values obtained without concurrent diazepam administration. The data indicated interference with phenytoin elimination by diazepam. The toxicity observed in the two patients presented in nystagmus, ataxia, dysarthria, lethargy, and inability to concentrate. It was reversible with reduction of the plasma phenytoin concentration. It is concluded that interaction between diazepam and phenytoin is of clinical significance, although its prevalence has yet to be determined. A similar interaction may apply to other benzodiazepines. 15 references. (Author abstract modified)

001827 Sakalis, G.; Chan, T. L.; Sathananthan, G.; Schooler, N.; Goldberg, S.; Gershon, S. Department of Psychiatry, New York University, 550 First Avenue, New York, NY 10016 **Relationships among clinical response, extrapyramidal syndrome and plasma chlorpromazine and metabolite ratios.** Communications in Psychopharmacology. 1(2):157-166, 1977.

The relationships among clinical response, extrapyramidal syndrome, and plasma chlorpromazine and metabolite ratios were examined in a study of hospitalized schizophrenic patients who received either chlorpromazine or a placebo and were clinically evaluated by psychiatric observation and tested for side-effects. Shortening of handwriting (micrographia) developed in nine out of 50 schizophrenic patients on a double-blind chlorpromazine vs. placebo study (33 of the patients received active medication). Another nine showed excellent clinical response but never exhibited shortening of handwriting. There was a wide interpatient variability in chlorpromazine plasma levels in agreement with previous reports, which did not differentiate between the two groups. However, patients with shortening of handwriting had higher 7hydroxychlorpromazine (7OHCPZ) plasma levels and two of them went on to develop clinically manifest extrapyramidal syndrome (EPS). 26 references. (Author abstract modified)

001828 Schuster, P.; Gabriel, E.; Kufferle, B.; Strobl, G.; Karobath, M. Psychiatrische Universitatsklinik, University of Vienna, Lazarettgasse 14, A-1090 Vienna, Austria **Reversal by physostigmine of clozapine-induced delirium.** Clinical Toxicology. 10(4):437-441, 1977.

Reversal of clozapine induced confusional reactions with i.v. infusion of physostigmine in two patients is described. A 25 year old manic female developed delirium upon receiving 100mg clozapine t.i.d.,and a 26-year-old male showed disorientation in time and space after a clozapine suicide attempt. It is noted that such confusional reactions usually occur during the first days of treatment with clozapine, and their incidence seems to be close to 10%. It is of interest that delirium occurred in the female patient treated with clozapine, who had no organic brain-damage, which is in contrast to the delirium induced by tricyclic antidepressants primarily in older patients and in patients with organic brain syndrome. Physostigmine, which can pass the blood-brain barrier, was effective in reversing the clozapine induced brain syndrome, and it also reduced one patient's tachycardia. 12 references.

001829 Segraves, R. Taylor. Dept. of Psychiatry, University of Chicago Hospitals and Clinics, Chicago, IL 60637 **Pharmacological agents causing sexual dysfunction.** Journal of Sex & Marital Therapy. 3(3):157-176, 1977.

Reports of pharmacological agents affecting the human sexual response cycle are critically reviewed. Topics discussed include: 1) effects of antipsychotic agents on ejaculation and erectile capacity; 2) antidepressants and ejaculation; 3) mood active drugs and erectile capacity; and 4) drugs affecting female sexual response. Because of the paucity of adequately designed studies, few definitive statements are made about pharmacological effects on human sexual functioning. Tentative evidence suggests that drugs with side-effects of adrenergic blockade are associated with ejaculatory disturbances. Im-

potence appears to be associated with drugs possessing significant anticholinergic activity. Drug induced impotence and retarded ejaculation could both also be related to central dopamine blockade. In view of the tentativeness of the findings, more double-blind experimental studies of the effects of drugs on sexual function are urged. 95 references. (Journal abstract modified)

001830 Shin, Kunishige; Takahashi, Shio; Kono, Tsuneo; Sato, Yutaka; Maruko, Kazuo; Kumashiro, Hisashi. Department of Neuropsychiatry, Fukushima University Medical School, Fukushima, Japan **Daily changes in the blood serum levels of diphenylhydantoin (DPH) and phenobarbital.** Psychiatria et Neurologia Japonica (Tokyo). 79(7):366, 1977.

In a report presented at the 31st Symposium for Northeastern Japanese Neuropsychiatrists held in October 1976 at the Miyagi Prefectural Doctor's Hall, changes in serum levels of diphenylhydantoin (DPH) and phenobarbital (PB) were measured over the period of a day to see if levels of these substances contributed to night movement and hearing difficulties often reported by users of these drugs. PB was investigated in 22 patients and DPH levels were measured in 9. All patients had been on the drugs for more than 3 months. Dosage was three times daily and serum levels were measured both before and after dosage. Results indicated no daily changes of significance in the serum levels of PB or DPH. The PB dosage was the more constant and stable of the two. The same dosage of DPH produced a wide variation of serum levels from individual to individual, and the results suggested that those with the higher blood levels were more prone to side-effects.

001831 Simpson, George M.; Lee, J. Hillary. USC Psychopharmacology Services, Norwalk, CA **The treatment of tardive dyskinesia.** Current Psychiatric Therapies. 17:235-245, 1977.

A discussion of tardive dyskinesia is presented, encompassing a description of the clinical features of the disease, with emphasis on early signs and their development, a survey of the literature on treatment, and a discussion of preventive measures. Clinical features include abnormal face, mouth and tongue movements (buccolingual masticatory syndrome) and choreoathetoid movements of the extremities. The results of studies on the treatment of tardive dyskinesia are reported, and it is pointed out that the lack of consistent or conclusive results may be related to a number of factors such as unclear diagnostic criteria, differences in the severity of this disorder as noted in long-term observation of an individual patient, and the unpredictability of drug reaction among patients. It is concluded that no satisfactory treatment has evolved from the research. Preventive measures suggested include: use of the lowest possible dosage of neuroleptics in patient maintenance; development of selection criteria of patients who might not require neuroleptic medication; the judicious use of other supportive drugs; the avoidance of using neuroleptic medications in the treatment of patients with depressions or anxiety neurosis; and the development and use of newer and "cleaner" drugs, such as the antipsychotic agents clozapine and lenperone which are now in the investigational stage. 49 references.

001832 Skolyarova, N. A. no address /**Gonadal morphology in schizophrenic patients under psychotropic treatment.**/ Morfologiya polovykh zhelez bol'nykh shizofreniyey v usloviyakh lecheniya psikhotropnymi preparatami. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 77(7):1043-1049, 1977.

A macroscopic and microscopic study was made of the genital glands in 33 schizophrenics (16 females and 17 males) receiving neuroleptic therapy. Most morphological studies of the gonads in schizophrenics were done before the current extensive use of psychotropic drugs and most reported glandular atrophy and depression of reproductive hormonal activity. The present material was obtained within 6 hrs of death. Normal histological picture of the ovary and testis was found in 12 cases, various degrees of involutional (atrophic) changes in 19, and tumor in 2. The degree of expressed histological modification was found to correlate with the age and duration of the disease, but not with the duration and intensity of psychopharmacotherapy. 6 references. (Journal abstract modified)

001833 Snyder, Richard. P. O. Box 333, Chepachet, RI 02814 **Haloperidol in barbiturate detoxification.** Military Medicine. 142(11):885-886, 1977.

A double-blind study to determine if the use of haloperidol during detoxification benefits the patient who is profoundly addicted to synthetic depressants, notably barbiturates, is presented. Data was obtained from 39 patients, 16 to 33 years old, forming two final groups of 17 test patients and 19 control patients. Of the 17 test patients, 13 were markedly improved within 5 days after withdrawal, four were not. Of the 19 patients in the control group, eight improved within the first 5 days, 11 patients did not. Patients in the test group had significantly fewer reactions to detoxification than those in the control group. It is suggested that haloperidol is a useful adjunct in detoxification of severely affected sedative addicts. 9 references.

001834 Sovner, Robert; Dimascio, Alberto. Tufts University School of Medicine, Medford, MA **The effect of benztropine mesylate in the rabbit syndrome and tardive dyskinesia.** American Journal of Psychiatry. 134(11):1301-1302, 1977.

A case of rabbit syndrome, a late onset neuroleptic induced extra pyramidal syndrome, is examined as syndrome apart from tardive dyskinesia. The patient, a 54-year-old woman, had received about 8 months of intermittent drug therapy for paranoid psychoses with several neuroleptic agents and had developed involuntary movements. Fluphenazine decanoate resolved the psychotic symptoms within several days, and involuntary movements decreased in severity. Assessment of involuntary movements confirmed a diagnosis of tardive dyskinesia, with perioral involvement. After development of severe mouth movements, benztropine mesylate was used to effect relief after which choreoathetoid movements of the extremities were observed. After discontinuation of benztropine mesylate, the mouth movements recurred and obliterated the more typical perioral and lingual movements of tardive dyskinesia. Benztropine mesylate i.v. did not affect the new movements, but increased the choreoathetoid movements. After changing to oral benztropine administered twice daily, the drug relieved the rabbit syndrome, but symptoms of tardive dyskinesia were again exacerbated. The response of the patient to benztropine mesylate (rabbit syndrome suppression and dyskinetic symptoms exacerbation) suggests clinical independence of these two neuroleptic side-effects. It was hypothesized that although drug induced parkinsonism and the rabbit syndrome are both mediated by neuroleptic blockade of dopaminergic neurons within the extrapyramidal system, the rabbit syndrome results only when this neuronal pool undergoes structural alteration. 7 references.

001835 Speight, A. N. P. Children's Department, Newcastle General Hospital, Newcastle Upon Tyne NE4 6BE, England

Floppy-infant syndrome and maternal diazepam and/or nitrazepam. The Lancet. No. 8043:878, 1977.

In a letter to the editor, the metabolism of diazepam in pregnant women is discussed. Administration of diazepam to the mother during labor can produce primary or secondary apnea, hypotonia, poor sucking, risk of aspiration of feeds, and hypothermia in the neonate. These complications are most common in infants whose mothers have been given more than 30mg diazepam in the 15 hours before delivery. Two case histories are presented to illustrate the postpartum sedation in the infant caused by a combination of diazepam and nitrazepam, and in one case by nitrazepam alone. There is a lack of awareness of the dangers of long-term diazepam use during pregnancy, and recommendations are made to alert the pediatric staff to the possibility of apnea and floppy infant syndrome in infants born to mothers who were maintained on diazepam during pregnancy and/or labor.

001836 Stambaugh, John E.; Wainer, Irving W.; Hemphill, Dorothea M.; Schwartz, Ira. Department of Pharmacology, Thomas Jefferson University, Philadelphia, PA 19107 **A potentially toxic drug interaction between Pethidine (meperidine) and phenobarbitone.** Lancet (London). No. 8008:398-399, 1977.

A case report of exaggerated meperidine toxicity in a patient receiving phenobarbital as an anticonvulsant is given, and this potentially toxic drug interaction is explored. The patient was a 31-year-old female given meperidine postoperatively after neuroblastoma removal as well as 30mg phenobarbital q.i.d. orally as prophylactic anticonvulsant therapy. After 2 weeks of phenobarbital therapy, the patient was again given meperidine and developed severe CNS toxicity. The patient was then given 30mg meperidine i.m. while still on phenobarbital, and urine samples were collected at 0, 0.5, 1, 2, 4, 6, 8, 24, and 48 hr postdrug. Lethargy was noted during the first 6 hr which began to clear by 8 to 10 hr. Urine was also collected in four patients receiving meperidine but not phenobarbital and in a normal volunteer given meperidine after 2 weeks pretreatment with 30mg phenobarbital q.i.d. orally. No significant differences in serum meperidine were observed in any of the subjects studied. Results indicate that phenobarbital induces the N-demethylation of meperidine, causing formation of toxic norpethidine. 5 references.

001837 Summa, J.-D. Stadt. Krankenanstalten Nurnberg, Nurnberg, Germany **Hypepinephria in cases of strong intoxication.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):193-196, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, the therapeutic consequences of adrenocortical insufficiency in heavy drug intoxication is discussed following an examination of 66 suicidal drug intoxications. Drug induced ACTH stimulation studies in 53 of these patients indicated that, particularly in older patients, inadequate response to recovery from heavy drug intoxication is due to adrenocortical insufficiency. Temporary administration of steroids is suggested.

001838 Thorstrand, C. Sodersjukhuset, Stockholm, Sweden **Hemodynamic effects following toxic doses of tricyclic antidepressants.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):48, 1977.

In a paper presented at the 7th International Congress of the European Association of Poison Control Centres, held at Oslo, Norway during June 1976, the hemodynamic effects following toxic doses of tricyclic antidepressants are described. Central hemodynamics were studied in 10 acute poisonings by tricyclic antidepressants and the peripheral effect of intraarterial infusion of the tricyclic compound amitriptyline was studied in seven healthy volunteers. The hyperkinetic circulation during moderate poisonings may be explained by adrenergic effects as well as a primary peripheral vasodilative effect of the drug with a subsequent increase in cardiac output. The latter assumption agrees with the finding of vasodilation, following intraarterial infusion of amitriptyline in doses resulting in locally toxic plasma levels. 2 references. (Author abstract modified)

001839 Tonks, Clive M. St. Marys Hospital, London W2, England **Lithium intoxication induced by dieting and saunas.** British Medical Journal (London). No. 6099:1396-1397, 1977.

A case of lithium intoxication in a 60-year-old man induced by dieting and sauna baths is reported. The man, who had been treated for depression, was dieting and taking saunas to lose the weight gained as a result of his antidepressant medication. Lithium intoxication consisted of confusion, ataxia, and tremulousness; symptoms subsided after 1 week of increased diet and cessation of saunas. Written instructions for lithium patients which warn them against special diets are urged. 5 references.

001840 Uchiyama, Michiaki; Sobue, Itsuro; Komura, Kazumi; Suzuki, Masaya; Kohno, Keizo; Ito, Motoo. Department of Psychology, Nagoya University School of Letters, Nagoya, Japan **Influences of antianxiety drugs on perception.** Japanese Journal of Psychosomatic Medicine (Fukvoka). 17(4):234-239, 1977.

To analyze the side-effects of antianxiety drugs in various psychological functions, 20mg of medazepam, 6mg of diazepam, and an inactive placebo (luctose) were administered to ten male and female student subjects, self-ratings were taken for sleepiness and emotional somatic condition, and visual and visual motor functions were observed. Results indicated no statistically significant differences between the self-ratings or visual functions were found, except for reaction time, which increased after administration of medazepam and decreased after administration of diazepam. Under diazepam, many subjects' reaction times decreased to 100msec or less. On the self-ratings of emotional/somatic conditions, it was found that the subjects tended to be calm and loose in emotional state and dull in somatic condition after administration of the two drugs, but this was not to a statistically significant degree. 12 references. (Author abstract modified)

001841 Van Peteghem, C.; Heyndrickx, A.; Moulin, A. Department of Toxicology, State University of Ghent, Hospitaalstraat 13, B-9000 Ghent, Belgium **Rapid identification of hypnotics in emergency cases by computerized gas chromatography-mass spectrometry.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):212-218, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, the use of computerized gas chromatographic/mass spectrometry (GC-MS) methods for the rapid identification of hypnotics in emergency drug overdose cases is discussed. A system of GC-MS computer assisted analysis of barbiturate drugs from submicrogram samples of urine and stomach content is described, as is the procedure for conducting the tests. A data system is provided with a library of about 400 mass spectra of standard compounds, including barbiturates and N-methylated barbiturates, and the abbreviated spectra are stored such that the most intense peaks of the spectra,

divided into 52 segments, are registered to identify each compound. The spectra of the sample is similarly processed and abbreviated, and the data system matches those 52 points to choose the 10 most likely compounds, presented in descending order of similarity. The retention times of each peak on the chromatogram of the sample are compared with a table of standard retention times for further identification. 6 references. (Author abstract modified)

001842 Volans, G. N.; Vale, J. A.; Crome, P.; Widdop, B.; Goulding, R. no address **The role of charcoal haemoperfusion in the active management of poisoning.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):38-39, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, the relative merits of charcoal hemoperfusion in the active management of drug overdosage are compared with other poison patient treatments (i.e. forced diuresis, peritoneal dialysis and hemodialysis). Adverse effects of the use of activated charcoal hemoperfusion (charcoal embolism, thrombocytopenia, leucopenia, fibrinogen loss and pyrexial reactions) are shown to be reduced by using acrylic hydrogel coated charcoal. Out of 22 patients reported to be treated by this method, 19 survived and 3 died from hypoxic cerebral damage. Those who survived had no major side-effects. It is suggested that this method of treatment makes a substantial contribution toward recovery from drug overdosage, and is particularly efficacious in those cases who have taken short and medium acting barbiturates and nonbarbiturate hypnotics. (Author abstract modified)

001843 von Muhlendahl, K. E.; Hammersen, G.; Krienke, E. G. Universitats-Kinderklinik der FU Berlin, D-1000 Berlin, Germany /**Physostigmine treatment of anticholinergic poisoning.**/ Physostigminbehandlung bei Vergiftungen mit anticholinergischen Substanzen. Monatsschrift fur Kinderheilkunde (Berlin). 125(5):531-532, 1977.

The use of physostigmine as an antidote for anticholinergic intoxication was discussed in a paper presented at the 73rd Session of the German Society of Pediatricians, Cologne, 1976. Physostigmine was found to be most effective in CNS symptoms after poisoning by an anticholinergic drug or drugs that produce an anticholinergic secondary effect, such as tricyclic antidepressants, phenothiazines, and benzodiazepines. This effective use of physostigmine as an anticholinergic esterase blocker is illustrated by four case studies of accidental or suicidal poisoning. Physostigmine, being cardioinhibitory, must be judiciously administered, especially in the case of poisoning by tricyclic antidepressives, and the patient must be monitored by EKG. Dosages are outlined. 4 references.

001844 Wang, Stephen F.; Marlowe, Christopher L. Morristown Memorial Hospital, 100 Madison Avenue, Morristown, NJ 07960 **Treatment of phenothiazine overdosage with physostigmine.** Pediatrics. 59(2):301-303, 1977.

A case report is given of a 2 1/2-year-old boy who swallowed five 100mg tablets of chlorpromazine. The boy was rushed to the emergency room and given 10ml syrup of ipecac, which caused immediate emesis. At this time, which was 30 min after ingestion, blood pressure was 80/60, pulse was 128 and regular, and respiration was 32/min. Urine screening for phenothiazines was positive, and the child gradually became comatose. At 3 hr after ingestion, the child was given 0.5mg physostigmine i.v. over 5 min, at which time he awoke. An hour later, he again became unresponsive and was given another 0.5mg physostigmine. A third dose was given 6 1/2 hr after ingestion. By 12 hr after ingestion, the child was alert and awake and received no further medication. 15 references.

001845 Wasserman, G. S.; Green, V. A.; Baska, R. E. University of Missouri, Kansas City School of Medicine, Kansas City, MO 64108 **Status epilepticus or repetitive seizures following toxic ingestion.** Clinical Toxicology. 10(4):485, 1977.

Paper presented at the joint meeting of the American Academy of Clinical Toxicology, the American Association of Poison Control Centers, and the Canadian Academy of Clinical Toxicology, Seattle, 1976, reported on a study of status epilepticus or repetitive seizures following toxic ingestion of psychoactive drugs. Three children showed status epilepticus or repetitive seizures for approximately 2 hours before proper treatment was initiated. Two of the children had taken imipramine HCl (Tofranil), and the other was intoxicated by thioxanthene chlorprothixene (Taractan). All subjects completely recovered normal behavior within 24 to 72 hours. This excellent prognosis has not previously been emphasized in the literature. (Journal abstract modified)

001846 Wegner, James T.; Struve, Frederick A.; Kane, John M. Department of Psychiatry, Long Island Jewish-Hillside Medical Center, Glen Oaks, NY 11004 **The B-mitten EEG pattern and tardive dyskinesia: a possible association.** American Journal of Psychiatry. 134(10):1143-1145, 1977.

The possible association of the B-mitten EEG dysrhythmia pattern with tardive dyskinesia is reported. If preliminary findings are confirmed, this EEG pattern could be used to identify patients at high-risk for tardive dyskinesia, and prophylactic efforts could be made early in treatment. The subcortical mitten dysrhythmia may signal a vulnerability to dopaminergic dysregulation within nigrostriatal pathways, perhaps potentiating dopamine receptor hypersensitivity secondary to prolonged neuroleptic blockage. 8 references.

001847 Weiss, Brian L. Department of Psychiatry, University of Miami School of Medicine, Miami, FL 33152 **Hazards of antipsychotic drug use in nonpsychotic patients.** Southern Medical Journal. 70(11):1387, 1977.

The hazards of administration of antipsychotic drugs to nonpsychotic patients are discussed in a letter to the editor. Subclinical side-effects are described which may mimic the target symptoms of anxiety and thus lead to increased dosages. Tardive dyskinesia, a neurologic syndrome consisting of involuntary and repetitive movements, is noted as a possible side-effect of antipsychotic drugs after prolonged usage. It is suggested that the physician consider administering a benzodiazepine tricyclic combination rather than an antipsychotic or phenothiazine because of the danger of dyskinesias. 3 references.

001848 Weiss, Brian L.; Jacobson, Alan F.; Steinbook, Richard M.; Brauzer, Benjamin; Goldstein, Burton J. Division of Research, Dept. of Psychiatry, Univ. of Miami School of Medicine, P.O. Box 520875, Biscayne Annex, Miami, FL 33152 **Controlled comparison of trifluoperazine and chlordiazepoxide in the treatment of anxiety.** Current Therapeutic Research. 22(5, Sect. 1):635-643, 1977.

To further evaluate the efficacy of neuroleptic drugs in anxious, nonpsychotic outpatients, as well as to document the incidence of short-term neuroleptic side-effects in these patients, trifluoperazine was compared to chlordiazepoxide, and to placebo in a four week, double blind study. A total of 126 out-

patients began the study (42 in each group), and a battery of patient and physician rating instruments was used to assess symptomatology and to record the emergence of side-effects. Trifluoperazine appears to be less efficacious than chlordiazepoxide in ameliorating symptoms of anxiety, as measured by our physician rating scales. However, on several physician measures, the trifluoperazine patients demonstrated improvement which approached statistical significance. Side-effects were a major cause of premature termination in the trifluoperazine group. Drowsiness, akathisia, excitement and diarrhea were the most frequent phenothiazine side-effects. It is suggested that some of the apparent lack of efficacy of trifluoperazine might be due to the wide variance in individual tolerance to phenothiazine side-effects. 13 references. (Author abstract modified)

001849 Westerfield, Byron T.; Blouin, Robert A. Box 224, Confederate Memorial Medical Center, 1541 Kings Hwy., Shreveport, LA 71130 **Ethchlorvynol intoxication.** Southern Medical Journal. 70(8):1019-1020, 1977.

The case of a patient suffering from coma due to ethchlorvynol intoxication is presented. Ethchlorvynol intoxication can be confusing to diagnose because of the lack of correlation between blood levels of the drug and clinical status. In this case, the patient was in a coma for approximately 1 week, although he had a blood level of ethchlorvynol generally considered to be subtoxic. A history of suicide attempts and empty prescription bottles of ethchlorvynol and chlorazepate dipotassium were the primary indicators. After 19 days the patient had recovered sufficiently to be transferred to the psychiatry service. 5 references.

001850 White, Lloyd; DiMaio, Vincent J. M. Institute of Forensic Sciences, Dallas, TX 75235 **Intravenous propylhexedrine and sudden death.** New England Journal of Medicine. 297(19):1071, 1977.

In a letter to the editor, recent studies of sudden death caused by intravenous abuse of propylhexedrine, an alpha adrenergic sympathomimetic agent, are discussed. Studies have shown that abuse of this drug may be a previously unreported cause of pulmonary hypertension. It has been found that an injectable solution of propylhexedrine can be prepared with cotton pledgets removed from the preparation used in nasal inhalers sold over the counter. This drug was developed as a substitute for the amphetamine present in the widely abused amphetamine sulfate (Benzedrine) inhaler which is no longer produced. Pulmonary conditions found in nine sudden death victims are described. Clinicians are advised to be aware of propylhexedrine abuse as a possible cause of pulmonary hypertension or sudden, unexpected death. 2 references.

001851 Widerlov, E.; Sjostrom, R.; Soderberg, U. Psychiatric Research Centre, University of Uppsala, S-75017 Uppsala, Sweden **D.D.A.V.P. and lithium-induced polyuria/polydipsia.** Lancet (London). No. 8047:1080, 1977.

Treatment of prophylactic lithium induced polydipsia and polyuria with desaminocys1-D-arg8 vasopressin (DDAVP) is described for 11 manic-depressive women. DDAVP treatment spanned 2 to 12 days of two or three daily administrations (0.2to 0.4ml/adm). Nine of eleven patients experienced subjective relief in intensity of polyuria and polydipsia, and had lower urine volumes and reported lower fluid intake during the treatment than during the pretreatment period. It is suggested that DDAVP might be of some benefit in relieving symptoms of polyuria and polydipsia in patients on prophylactic lithium.

001852 Winters, W. D.; Johnson, M. Emergency Medicine, Sacramento Medical Center, Sacramento, CA 95817 **The tricyclic antidepressant overdosed patient.** Clinical Toxicology. 10(4):486-487, 1977.

Paper presented at the joint meeting of the American Academy of Clinical Toxicology, the American Association of Poison Control Centers, and the Canadian Academy of Clinical Toxicology, Seattle, 1976, discusses case histories of 25 patients overdosed with tricyclic antidepressants. The typical patient is a 28-year-old female who has ingested 1.5g amitriptyline, along with a hypnotic or alcohol. Patients were admitted with one of three types of symptoms: 1) mild tachycardia; 2) coma and/or convulsions with elevated blood pressure and heartrate above 140; or 3) coma and occasionally convulsions with reduced blood pressure and heartrate of 120. Nine patients with type 2 symptoms went on to type 3, usually within 1 to 4 hours of ingestion, and six patients with type 1 (average duration 2 hours) went on to type 2 or type 3. The latency of type 1 may be related to delayed gastric emptying into the duodenum, where maximal tricyclic antidepressant absorption occurs. Type 2 appears to be related to the norepinephrine uptake blocking properties of tricyclic antidepressant inducing excessive alpha and beta adrenergic stimulation, resulting in increased heartrate and blood pressure. The type 3 effect appears to occur when the catecholamine is out of synaptic areas and there is depletion of alpha sympathetic tone. Use of physostigmine and correction of acidosis with bicarbonate are essential for tricyclic antidepressant overdose treatment.

001853 Winters, Wallace D.; Ralph, David D. Section of Emergency Medicine, University of California at Davis, Davis, CA 95616 **Digoxin-lithium drug interaction.** Clinical Toxicology. 10(4):487-488, 1977.

Paper presented at the joint meeting of the American Academy of Clinical Toxicology, the American Association of Poison Control Centers, and the Canadian Academy of Clinical Toxicology, Seattle, 1976, reported on digoxin/lithium drug interaction resulting in increasing tremulousness, marked confusion, and a severe nodal bradycardia alternating with slow atrial fibrillation in a patient taking commonly used dosages of both drugs. The lithium blood level was in the toxic range and the dogoxin level was in the lower therapeutic range at the time of admission. Despite discontinuation of both medicines the heartrate fell to 30/min the following day, requiring placement of a temporary pacemaker for 6 days before the patient reverted to normal sinus rhythm. Findings suggest that the intracellular potassium depletion caused by lithium potentiated the effect of digoxin and thus led to synergistic toxic effect resulting in prolonged arrhythmia.

001854 Yamada, Kayoo; Ishimaru, Toranosuke. Department of Psychiatry, Yamaguchi University, Japan **Syndrome malin symptoms thought to be due to interaction between neuroleptics and oral diabetes drugs.** Psychiatria et Neurologia Japonica (Tokyo). 79(4):206, 1977.

At the 26th Central Japan Shikoku Symposium of Neuropsychiatrists, November 1976, Okayama, Japan, a case history was presented of a 47-year-old man who during thiothixene and periciazine treatment for diabetes developed schizophrenia. Upon being treated with chlorpropamide, he became confused, had increased muscle tension and fast heartrate, sweated, drooled, ran a high fever, and died after 10 days. There was no autopsy, but before death liver function, brain wave, and spinal fluid tests showed no notable abnormalities. Another female patient developed the same type of

symptoms with the combination of fluphenazine enanthate, perazine, periciazine, and chlorpropamide. She was taken off chlorpropamide and recovered after 2 weeks. Both cases showed hypoglycemia with the chlorpromide. It was considered possible that the oral diabetes drugs contributed to the development of syndrome malin.

16 METHODS DEVELOPMENT

001855 Amin, M. M.; Ban, T. A.; Lehmann, H. E. McGill University, Montreal, Quebec, Canada **Desipramine in the treatment of depression: a comparison of divided vs single dose administration.** Psychiatric Journal of the University of Ottawa (Ottawa). 2(3):117-119, 1977.

Comparison of divided versus single dose administration of desipramine in the treatment of depression carried out in a double-blind experiment with 20 psychiatric depressive outpatients is described. Results showed that clinically, single dose administration was as effective as a divided dose regimen. Findings also showed that a change from divided to single dose and vice versa did not result in any deterioration of the depressive psychopathology. No obvious difference was found in adverse effects in the two groups. A positive correlation was found between plasma levels and therapeutic efficacy. 5 references.

001856 Asano, Hiroki; Shinoda, Kazuo. Department of Neuropsychiatry, Tohoku University, Tohoku, Japan **Looking toward a reexamination of drug therapy experience.** Psychiatria et Neurologia Japonica (Tokyo). 79(7):371, 1977.

At the 31st Symposium for Northeastern Japanese Neuropsychiatrists held in October 1976 at the Miyagi Prefectural Doctor's Hall, the results of studying local psychiatric magazines in a controlled study for a 20 year period to assess the administration of psychotropic drugs during that period were presented. It was found that about 30% of the cases had been given mistaken drug therapy by today's standards, and further that there was no real consensus on the type of treatment and the malady. There was not sufficient time to study side-effects of the various drugs, nor examine any possible deaths caused by the drug therapy.

001857 Bombardt, Paul A.; Friedel, Robert O. Dept. of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA 98195 **A GC/CIMS assay for the CIS and TRANS isomers of thiothixene in human plasma.** Communications in Psychopharmacology. 1(1):49-59, 1977.

A sensitive gas chromatography/mass spectrometric assay for monitoring electron impact fragments (GC/EIMS) in the determination of thiothixene is described. Use of cis-trideuterothiothixene as the internal standard allowed plasma levels as low as 1ng/ml to be quantified with a high degree of precision. This assay permits the separation of pharmacologically active cis-thiothixene from the relatively inactive trans form. Plasma drug levels from patients treated with cis-thiothixene suggest conversion in vivo of the cis to the trans isomer by an unknown mechanism. 9 references. (Author abstract modified)

001858 Brodie, R. R.; Chasseaud, L. F.; Crampton, E. L.; Hawkins, D. R.; Risdall, P. C. Dept. of Metabolism and Pharmacokinetics, Huntingdon Research Centre, Huntingdon, England **High performance liquid chromatographic determination of dothiepin and northiaden in human plasma and serum.** Journal of International Medical Research (Northhampton). 5(6):387-390, 1977.

A method developed for the separation and measurement of dothiepin, a tricyclic antidepressant, and the N-desmethyl metabolite, northiaden, in human plasma or serum by high performance liquid chromatography is described. The method uses a structurally related drug, amitriptyline, as an internal standard and provides a limit of detection of about 10ng/ml for each component. At a concentration of 20ng/ml, northiaden and dothiepin could be measured within 11% and 6% of the mean respectively and at 200ng/ml within 3% and 1% of the mean. The method has been applied to the analysis of serum from patients undergoing dothiepin therapy. 5 references. (Author abstract)

001859 Brunswick, D. J.; Mendels, J. Veterans Hospital, Philadelphia, PA 19104 **Reduced levels of tricyclic antidepressants in plasma from Vacutainers.** Communications in Psychopharmacology. 1(2):131-134, 1977.

The effect of the use of Vacutainers for blood sample collection on the plasma levels or the extent of plasma protein binding of tricyclic antidepressants was measured in experiments comparing imipramine (IMI) plasma levels of blood held in Vacutainers and other types of containers. In one experiment, therapeutic concentrations of IMI were added to the blood of healthy volunteers. The blood samples were then removed to Vacutainers, polystyrene tubes, or siliconized glass tubes. The blood was centrifuged and plasma IMI concentrations were measured by radioimmunoassay. Results showed that plasma levels in the Vacutainers fell off by up to 50% compared to both polystyrene and glass. It was found that contact with the rubber stopper of the Vacutainer caused the plasma level drop. In another experiment, blood was collected from a patient being treated with desmethylimipramine (DMI). Blood drawn into a plastic tube had a 50% higher DMI plasma concentration than that transferred to a Vacutainer. It is concluded that the use of Vacutainers should be avoided for collection of blood samples for tricyclics and other basic lipophilic drugs. 6 references.

001860 Dhar, A. K.; Kutt, H. Department of Neurology, Cornell University Medical College, New York, NY 10021 **Blood level monitoring of benzodiazepines by GLC using nitrogen sensitive detectors.** Pharmacologist. 19(2):182, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, a method for monitoring blood levels of benzodiazepines by gas/liquid chromatography was reported. The method uses a nitrogen sensitive detector, which permits use of a small volume of plasma and high sensitivity setting for the detector at low background noise. The method yields reliable reproducibility, and other anticonvulsants do not cause interfering peaks. Plasma levels of 5ng/ml to 30ng/ml of clonazepam and 50ng/ml to 1200ng/ml of diazepam were detected in samples of 0.5ml or 1ml of buffered human plasma. 1 reference. (Author abstract modified)

001861 Erban, L.; Kalvach, Z.; Peckova, E. Psychiatric Research Institute, Prague 8, Czechoslovakia **Chlorpromazine induced changes in blood adenosinephosphoric acids: to their diagnostic significance in psychiatry.** Activitas Nervosa Superior (Praha). 19(3):178-179, 1977.

The chlorpromazine dose necessary for the increase of blood concentrations of adenosinephosphoric acids in vitro was established and correlated with clinical data in an attempt to determine a relationship between the effective dose of chlorpromazine and psychiatric diagnosis and prognosis. The subjects were 40 psychiatric inpatients who had been under no

active therapy for at least 1 week. Concentrations of adenosinephosphoric acids were measured before application of chlorpromazine and 1, 2, 4, and 12 minutes after its administration. No relationship was found between the total duration of previous hospitalization or gross clinical diagnosis and the effective dose of chlorpromazine. It is concluded that objective criteria, such as number of readmissions, number and duration of hospitalizations, and gross clinical diagnosis, remain as the diagnostically significant factors in prognosis.

001862 Hachey, D. L.; Kreek, M. J.; Mattson, D. H. Division of Biological and Medical Research, Argonne National Laboratory, Argonne, IL 60439 **Quantitative analysis of methadone in biological fluids using deuterium-labeled methadone and GLC-chemical-ionization mass spectrometry.** Journal of Pharmaceutical Sciences. 66(11):1579-1582, 1977.

A method for the quantitative analysis of methadone in biological fluids using deuterium labeled methadone and gas liquid chromatography (GLC) chemical ionization mass spectrometry is described. The synthesis of the dextrorotatory, levorotatory, and racemic deuterium labeled methadones containing five deuterium atoms in one aromatic ring is also described. These compounds were used in clinical pharmacological studies and as internal standards. The method described can measure plasma drug levels of 10picomoles/ml and urine levels of 5picomoles/ml. Plasma methadone levels were examined in several patients undergoing methadone maintenance therapy. The levels generally ranged between 100 and 400nanograms/ml (320 to 1300picomoles/ml) after an average oral dose of 1mg/kg/day. The methadone half-life was about 29 hr. It is posited that the method will permit more accurate measurement of low methadone levels present in adolescent addicts on methadone maintenance therapy and in infants of mothers maintained on methadone, and that the method may also be useful in animal studies in which plasma methadone levels are lower and turnover rates are much faster than in humans. 21 references. (Author abstract modified)

001863 Hollister, Leo E. Stanford Univ. School of Medicine, Palo Alto, CA 94305 **Individualised dosage of tricyclic antidepressants.** Current Therapeutics (Seaforth). 18(9):11-12, 1977.

In an editorial, an approach to individualized dosage of tricyclic antidepressants is presented, which begins with small doses followed by frequent increments until either the desired amelioration of depression is reached, or the presence of unwanted effects makes further increases intolerable. Undertreatment is the most common cause of poor results with the trycyclics. A minimum dose of 75mg/day is suggested for otherwise healthy patients, with additional 25mg daily dose increments during the first several days to attain a dose of 150mg/day. Reassessment is then suggested to reconsider the diagnosis, the choice of drug, and the need to increase the dose further. 7 references.

001864 Immich, H. Inst. fur Med. Dok., Stat. und Datenverarb. der Univ., Im Neuenheimer Feld 325, D-6900 Heidelberg, Germany **/Statistical evaluation: presumption and methods./** Statistische Auswertung: Voraussetzungen und Methoden. Pharmakopsychiatrie/Neuro-Psychopharmakologie (Stuttgart). 10(3):185-192, 1977.

The role of statistics in the planning stage of psychotropic drug trials is examined. It is suggested that the test plan is incomplete unless certain null hypotheses are advanced for subsequent disproof by test results. Prior identification of nonspecific factors is helpful, with the aid of statistical methods. It is concluded that factors that cannot be held constant are best removed. Criteria used in comparisons can work only if they are relevant to the methods being tested, and all criteria must be replicable. To prevent random correlations, the number of independent criteria is reduced to a minimum. During the trial, randomization is strictly maintained; the first step in evaluation is a confirmation of randomization by comparison with initial data. Various statistical methods are applied to lag times, dosage effects, and the distribution of process curves. It is concluded that in view of subjective syndrome descriptions and final evaluations provided by psychiatrists, statistics alone cannot decide on the degree of improvement attributed to the drug. 11 references.

001865 Inomata, Yoshimasa; Aizawa, Hirnkuni; Endo, Yasu; Kikuchi, Jun. Miyagi Prefectural Natori Hospital, Miyagi, Japan **On long-term maintenance of psychotropic drug therapy: the combined administration of anti-Parkinson's drugs.** Psychiatria et Neurologia Japonica (Tokyo). 79(7):370, 1977.

At the 31st Symposium for Northeastern Japanese Neuropsychiatrists held in October 1976 at the Miyagi Prefectural Doctor's Hall, results of eliminating the anti-Parkinson's drugs and investigating extrapyramidal (EPS) symptoms were reported in 120 patients who had been taking these drugs in conjunction with their regular therapy. EPS appeared in 10% of the men and in 26.7% of the women. Only 13 of these patients were placed back on anti-Parkinson's drugs. It was found that EPS were more prevalent in those also taking Butyrophenone type drugs (26.7%) than in those taking Phenothiazine type (13.2%). The Biperiden type of anti-Parkinson's drugs caused more EPS symptoms (22.5%) upon withdrawal than did the Promethazine type drugs (12.2%).

001866 James, Margaret F. West Cumberland Hospital, Whitehaven, Cumbria, England **Guidelines for nurses: the administration of intravenous drugs through an established intravenous pathway.** Nursing Mirror (Surrey). 154(19):viii, x, 1977.

Guidelines for nurses in the administration of intravenous drugs through an established intravenous pathway are presented. The guidelines emphasize the double check system of drug procedures, specifically making sure that the drug selected is of intravenous variety, not out of date, that literature on the dilution quantity, type of solvent, and rate to be given are supplied. The drug incompatibilities in the patient's prescription should be double checked. Actual drug administration procedures are enumerated and factors and symptoms during the procedure are discussed.

001867 Langer, Gerhard; Sachar, Edward J.; Halpern, Frieda S.; Gruen, Peter H.; Solomon, Murray. Dept of Psychiatry, Columbia University College of Physicians & Surgeons, 722 West 168th St., New York, NY 10032 **The prolactin response to neuroleptic drugs. A test of dopaminergic blockade: neuroendocrine studies in normal men.** Journal of Clinical Endocrinology and Metabolism. 45(5):996-1002, 1977.

The tonic inhibition of prolactin (PRL) secretion and the heuristic potential of this PRL response as a neuroendocrine model for studying hypothalamic/pituitary regulation in man were investigated. Nineteen normal young men were studied in a series of weekly experiments; at each session a single drug and dose, out of seven neuroleptic drugs in various doses, was given parenterally. Plasma PRL concentrations were then monitored for at least 3 h. Repeated administrations of haloperidol and prochlorperazine demonstrated a high reproducibility of the PRL response within a subject. The PRL

response to four doses of haloperidol showed a sigmoid dose responsive curve. Dose PRL response curves of haloperidol, prochlorperazine, and thiothixene, representing three chemical classes of neuroleptic drugs, showed a parallel relationship. This suggests a common pharmacological, very likely antidopaminergic, mechanism of the drugs when releasing PRL. In response to haloperidol, chlorpromazine, and trifluoperazine plasma PRL concentrations remained elevated for at least 7 h, consistent with reported plasma half-lives of these drugs. The data indicate that the PRL response to neuroleptic drugs is sensitive and reliable and is probably a valid test of dopaminergic blockade in man, and suggest a model for studying drug and hormonal interactions with neuroleptics in man. 17 references. (Author abstract modified)

001868 Lipton, Morris A. Child Development Research Institute, School of Medicine, Univ. of North Carolina, Chapel Hill, NC 27514 **Pharmacological research and the psychoses: an overview.** In: NIMH, Research on disorders of the mind: progress & prospects. Rockville, MD, NIMH, 1977. 54 p. (p. 24-25).

A paper, in condensed version, delivered at the 100th meeting of the National Advisory Mental Health Council on pharmacological research and the psychoses is presented. A need for deriving genetic markers, perhaps from biochemical research, is cited. In the area of schizophrenia, improvement is suggested through the development of better drugs with fewer side-effects. Additional research into rational combinations of drugs based on how the brain acts also is needed.

001869 London, Jack W.; Burns, David; Frazer, Alan; Brunswick, David; Garfinkel, David; Mendels, Joe. Department of Computer and Information Science, University of Pennsylvania, Philadelphia, PA 19104 **Computer simulation of the movement of lithium across erythrocyte membranes in vitro.** Communications in Psychopharmacology. 1(3):271-282, 1977.

Computer simulation of data obtained from in vitro lithium uptake experiments was used to define influx and efflux components of the net flux of lithium transport across human erythrocyte membranes. The variation in in vitro erythrocyte to medium lithium distribution ratios for different individuals appears to be primarily due to the efflux component. Furthermore, subjects with a high erythrocyte to medium lithium concentration ratio had lower rates of both lithium influx and efflux than other subjects, implying that low rates of lithium efflux from erythrocytes cause certain individuals to exhibit high distribution ratios. 10 references. (Journal abstract)

001870 Post, Robert M.; Jimerson, D. C.; Bunney, W. E., Jr. Adult Psychiatry Branch, Room 3S239, Building 10, NIMH, Bethesda, MD 20014 **Perspectives in the treatment of the psychoneurological disorders: affective disorders. (Unpublished paper).** Bethesda, MD, NIMH, 1977. 13 p.

Current research strategies in the pharmacotherapy of the affective disorders are reviewed, highlighting major trends and areas of particular promise. Some progress is reported toward the identification of biologically defined subgroups by assessing amine metabolites in urine or cerebrospinal fluid which may lead to a more rational choice of therapies for depressed patients. The use of drugs with receptor agonist properties may help define biological substrates altered in affective illness and lead to new approaches to treatment, such as utilization of low doses of receptor agonists which may preferentially stimulate presynaptic receptors. It is suggested that study of time dependent and adaptive changes in receptor sensitivity may also add an important perspective in conceptualizing the cyclic process in manic-depressive illness and its treatment. 72 references. (Author abstract modified)

001871 Rivera-Calimlim, Leonor; Siracusa, Alan. Department of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **Plasma assay of fluphenazine.** Communications in Psychopharmacology. 1(3):233-242, 1977.

A gas liquid chromatographic method for the assay of plasma fluphenazine was developed. The accuracy and reproducibility of the assay were demonstrated by serial dilution curves with a correlation coefficient of r equals 0.97. The sensitivity of the assay is 3ng/ml plasma; that of the detector, 1ng. Some factors that can lead to falsely low plasma values are discussed. The development of an assay for plasma fluphenazine with reliability and accuracy provides a valuable tool for the study of the plasma pharmacokinetics of fluphenazine in psychiatric patients. 19 references. (Journal abstract modified)

001872 Sato, Tami; Aizawa, Hirokuni; Inomata, Yoshimasa; Endo, Yasu. Miyagi Prefectural Natori Hospital, Miyagi, Japan **A debate on maintenance of psychotropic drug therapy -- reflections on the so-called long-term saturation administrations.** Psychiatria et Neurologia Japonica (Tokyo). 79(7):370, 1977.

At the 31st Symposium for Northeastern Japanese Neuropsychiatrists held in October 1976 at the Miyagi Prefectural Doctor's Hall, long-term administration of psychotropic drugs was discussed in light of an attempt to gradually reduce medication for 25 chronic schizophrenic patients. The reduction in medication was carried out until the patients' conditions worsened. Five patients were completely taken off medication without bad effects, and another 8 could maintain a good condition with as little as 20mg of thioridazine. Twelve of the patients did relapse into a worsened condition, but by restoring medication, they were easily brought back to their previous level. Six of the patients were released from the hospital after lowering the amount of medication, but their progress was not easy. It was concluded that decreasing the level of medication in chronic patients was not the only answer to their problems.

001873 Wang, Richard I. H.; Stockdale, Susan L. VA Center, Wood, WI **A subjective and objective method assessing the efficacy of hypnotic medications in insomniacs.** Journal of Clinical Pharmacology. 17(11&12):728-733, 1977.

The response of chronic insomniacs to 100mg pentobarbital, 300mg methyprylon, 500mg glutethimide, and placebo was assessed using previously described subjective and objective techniques. The purpose of the study was to examine: 1) the presence or absence of the subjects' reported insomnia; 2) the subjects' ability to discriminate between active hypnotic drugs and placebo; and 3) whether any preference existed among active medications. Statistically significant finding included a high degree of correlation between subjective and objective data and greater response to active medications as compared to placebo shown on all parameters except objective onset of sleep. In no case was there significant difference between the two nights of placebo. Although methyprylon was most frequently superior to placebo, there was no significant patient preference for any of the active medications. 9 references. (Author abstract)

001874 Yahaba, Yoshio. Department of Neuropsychiatry, Akita University, Akita, Japan **A reexamination of using anti-Parkinson's drugs with psychotropic drug therapy -- a survey of outpatients.** Psychiatria et Neurologia Japonica (Tokyo). 79(7):370-371, 1977.

At the 31st Symposium for Northeastern Japanese Neuropsychiatrists held in October 1976 at the Miyagi Prefectural Doctor's Hall, results of surveying 163 outpatients who were taking both psychotropic drugs and anti-Parkinson's drugs were presented. A full 90% of those patients were taking the anti-Parkinson's drugs on an indefinite basis. Some patients (n=85) were taken off of the Parkinson's medication and the results were observed. Only 12 patients (14%) complained of a worsening of their symptoms and only 2% complained of Parkinson's symptoms. It was thought that the other 10 patients were relying on the psychological value of the medication or its sleep inducing properties. As a result of these findings, several criticisms were leveled at the long-term prescription of anti-ParkinsonS drugs in conjunction with conventional medication.

001875 Yatzkan, Amy. no address **Toward an ego-oriented approach to the study of the effects of psychoactive medication in the treatment of children.** Smith College Studies in Social Work. 48(1):43, 1977.

The effect that treatment with psychoactive medication has on children is studied with regard to influences on the development of the ego. Methodological limitations in the research of psychopharmacology are critiqued and illustrated. It is stated that published research has shown a general disregard for the developmental issue of childhood and that knowledge of children's expressed fantasies could be a valuable adjunct to future psychopharmacological research and could alleviate some of the problems currently existing in drug research with children. Methods for eliciting the necessary fantasy material are suggested, and it is concluded that such data would measure ego development as it is reflected in the fantasy content.

001876 Zavadil, Anthony P., III; Potter, W. Z.; Kopin, I. J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Prediction of plasma levels of imipramine from pharmacokinetics of an initial dose. (Unpublished paper).** Bethesda, MD, NIMH, 1977. 1 p.

A single oral dose of imipramine was administered to six patients to determine whether the dose of drug required to yield a given plasma level could be predicted from the pharmacokinetics of an initial dose of the drug. The levels of the test drug and its metabolite, desipramine, were measured in plasma by a gas chromatography/mass spectrometric method. The areas under the plasma concentrations vs time curve after this single dose were used to predict the steady state concentrations of the drug. The ratio of predicted steady state concentration to that found in the plasma was 1.01. It is suggested that plasma clearance rates of imipramine do not vary significantly over a relatively wide range of concentrations and that plasma levels of the chronically administered drug can be predicted from the pharmacokinetic behavior of the first dose. 1 reference. (Author abstract modified)

17 MISCELLANEOUS

001877 Adelman, Howard S.; Compas, Bruce E. Fernald School, Psychology Dept., UCLA, Los Angeles, CA 90024 **Stimulant drugs and learning problems.** Journal of Special Education. 11(4):377-416, 1977.

A review of stimulant drug research as it relates to learning problems, which highlights the problem of experimental procedures being prematurely applied despite a lack of proven treatment efficacy, is presented. Critical analysis indicates no satisfactory support for the efficacy of stimulants in improving academic learning and performance or behavior problems, and no data regarding the possibility of long-term negative side-effects. Amphetamines administered to persons with learning problems are seen as producing the common effects usually attributed to such stimulants. These include mild to moderate improvement in nonacademic performance, concomitant reductions in activity, and shortening of response latency on tasks characterized as repetitious, mechanical, regulated by an external agent, and requiring concentration and sustained performance. Evidence has not clarified the generalizability or state dependency of such effects. Complex behavior, such as reasoning, problem solving, and socioemotional functioning, do not seem affected. Widespread use of drugs for learning problems is seen as premature and, until possible side-effects are clarified, perhaps dangerous. 143 references.

001878 Atkinson, Leigh; Gibson, Iris I. J. M.; Andrews, James. London School of Occupational Therapy, London, England **The difficulties of old people taking drugs.** Age and Ageing (London). 6(3):144-150, 1977.

The causes of faulty taking of prescribed drugs by elderly patients are identified and discussed with suggestions concerning future improvements. In many cases elderly patients, though given detailed instructions regarding bathing, eating, walking, and sleeping habits, are given virtually no instructions concerning the proper means of taking the drugs which are prescribed for them on an outpatient basis. Seventy one percent of hospital admissions have been said to be due to drug reactions. Failing eyesight, poor memory, a tendency towards confused thought and the inability to handle containers may all contribute to the difficulties which old people can have in management of their drug taking schedule. Solutions to the problem may include simpler package designs, investigations concerning the effects which color, shape, and taste of the drug unit have on drug taking behavior, and more thorough education in drug handling for elderly patients. 34 references.

001879 Ayd, Frank J., Jr. Taylor Manor Hospital, Ellicott City, MD **Loxapine update: 1966-1976.** Diseases of the Nervous System. 38(11):883-887, 1977.

A summary and update of current knowledge of assets and liabilities of loxapine succinate based on clinical experience, personal communications, and published reports, is presented. Since the mid-1950s, an incessant search for new neuroleptics has resulted in a variety of these compounds belonging to different chemical groups -- phenothiazines, butyrophenones, thioxanthenes, and dihydroindolones. A recent additon to this catalog of antipsychotics is loxapine succinate, the first of a series of dibenzoxazepine compounds. These are not structurally related to the other classes of neuroleptics, although pharmacologically loxapine has properties similar to those of known neuroleptics. It was first tested clinically in 1966 by Bente and his associates in Germany. Since then loxapine has been administered to several thousand patients, for a few days to as long as three years or more, in both uncontrolled and well designed controlled clinical trials, including a multihospital international collaborative study. 50 references. (Author abstract modified)

001880 Baldessarini, Ross J. no address **Chemotherapy in psychiatry.** Cambridge, MA, Harvard University, 1977. 196 p. $9.95.

Descriptions, chemical structures, and the uses of various psychopharmacological agents are presented. Information in the volume is organized according to drug types starting with antipsychotic agents and continuing through lithium salts, antidepressant agents, and antianxiety drugs with special attention to geriatric and pediatric psychopharmacology. Detailed recommendations for use of each drug include discussions of toxicity and side-effects, and an assessment of relative dosage strengths. A comprehensive bibliography is included.

001881 Baldessarini, Ross J. Massachusetts General Hospital, Mill St., Belmont, MA 02178 **Schizophrenia.** New England Journal of Medicine. 297(18):988-995, 1977.

The treatment of schizophrenia, a common and severe mental illness of unknown cause characterized by disturbances of mood, thinking, and behavior in the face of relatively clear sensorium, is reviewed. Since the 1950s, the introduction of drugs and associated changes in the pattern of delivery of psychiatric care have led to striking reductions in prolonged hospital care, and increased optimism about the treatability of the illness. Studies of antipsychotic drugs have led to impressive strides in the application of neurobiological techniques to preclinical and clinical biological psychiatry. A coherent theory of the interactions of antipsychotic agents with central dopamine receptors is emerging, although as yet this has led to few practical innovations in the development of improved drugs. 8 references.

001882 Balkrishna, V.; Sanghvi, L. D.; Rana, K.; Doongaji, D. R.; Vahia, N. S. Cancer Research Institute, Bombay, India **The comparison of psychophysiological therapy with drug therapy.** Indian Journal of Psychiatry (Poona). 19(2):87-91, 1977.

A comparison of psychophysiological therapy and drug therapy in psychoneurotic disorders was conducted. The psychophysiological treatment was given to 34 patients and consisted of five steps of Yoga therapy given 6 times a week for 2 months. Forty one patients completed the drug treatment. No significant difference between the two groups was found on Taylor's Manifest Anxiety Scale (TMA), Hamilton's Depression Scale (HD), and Bell's Social Adaptation Scale (BSA). However, in all cases the average ranks were slightly higher for the psychophysiological therapy group, and it is indicated that this treatment is more effective than drug therapy when improvement is measured by reduction in scores on the TMA or BSA. The results suggest that psychophysiological therapy is useful in stress induced psychological disturbances and that is better than drug therapy in curing, rather than alleviating, the symptoms of the disease. 10 references.

001883 Bellak, Leopold. Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461 **A drug-free week after admission.** Schizophrenia Bulletin. 3(3):342-344, 1977.

An editorial concerning the diagnostic problems which can occur when schizophrenic patients are treated with drugs such as phenothiazine immediately upon their admission to a psychiatric emergency room is presented. Since schizophrenic syndrome consists of many etiologic, pathogenic, and clinical subgroups, there is a risk of obliterating all clinical distinctions by immediate phenothiazines and other neuroleptics to the point where differential diagnostic observations cannot be made. The suggestion is made that all psychiatric patients be kept drug free for 1 week after admission for diagnostic appraisal. 8 references.

001884 Biggs, John T.; Ziegler, Vincent E. Washington University School of Medicine, St. Louis, MO **Tricyclic antidepressants in outpatient therapy.** Current Psychiatric Therapies. 17:171-178, 1977.

Tricyclic antidepressants in outpatient therapy of depression are discussed, and data on optimal therapeutic plasma levels and antidepressant response are presented. The importance of providing the clinician with insight into patient drug compliance and individual differences in drug metabolism through collection and interpretation of clinical data is emphasized. It is noted that evaluative tricyclic plasma measurement must address the following questions: 1) Is the medicine being ingested as prescribed? 2) Is the patient a rapid or slow drug metabolizer? 3) Is the patient unresponsive to a specific antidepressant? 4) Are side effects due to the medication or to symptoms of the depression? and 5) Is abuse of the medication contributing to the patient's psychiatric state? Medication scheduling and dosage alteration in the use of tricyclics (amitriptyline, desipramine, doxepin, imipramine, nortriptyline and protriptyline) on an outpatient basis are described. 25 references.

001885 Bigler, Erin D. Austin State Hospital, 4110 Guadalupe, Austin, TX 78751 **Neurophysiology, neuropharmacology and behavioral relationships of visual system evoked after-discharges: a review.** Biobehavioral Reviews. 1(2):95-112, 1977.

Visually evoked response (VER) afterdischarge (AD) research in animals and humans is reviewed, neurophysiological and neuroanatomical contributions are developed in terms of the thalamic generating mechanisms of VER ADs, and the association between a variety of brain systems in terms of the modulation and functional significance of the VER AD is provided. The neuropharmacology of VER ADs is likewise examined with respect to the development of an experimental epilepsy model, this being dependent upon the observations that convulsants markedly augment while anticonvulsants significantly attenuate VER ADs. Cholinergic and catecholaminergic systems are also discussed in terms of their relevancy with the neuropharmacology of VER ADs. A unifying theme of the behavioral research associated with VER AD elicitation and elaboration has been with an underlying arousal dimension. The multidisciplinary approach taken by VER AD research suggests the direct application of this type of orientation for a variety of behavioral research areas. 303 references. (Author abstract modified)

001886 Casey, Daniel E. Departments of Medical Research and Psychiatry, VA Hospital, Portland, OR **Deanol in the management of involuntary movement disorders: a review.** Diseases of the Nervous System. 38(12, Section 2):7-15, 1977.

The use of deanol acetamidobenzoate in the management of involuntary movement disorders is reviewed. In the past decade important advancements have been made in understanding the role dopaminergic and acetylcholinergic influences play in involuntary movement disorders. Deanol, because of its ability to increase CNS acetylcholine, recently has been used to treat the dyskinetic symptoms associated with tardive dyskinesia, levodopa induced dyskinesias, Huntington's disease and a few other uncommon dyskinesias. Until more data are collected the role of deanol in the treatment of involuntary movement disorders must remain open. In the interim, deanol is an important tool for investigating the function of acetylcholine in the CNS, and it provides a potential treatment for dyskinetic symptoms which are often disabling and at present have disappointing therapies. 58 references. (Author abstract modified)

001887 Celesia, Gastone G. Department of Neurology, St. Louis University, St. Louis, MO **Therapy of Parkinsonism.** Current Psychiatric Therapies. 17:219-225, 1977.

The pharmacotherapy of Parkinsonism is described, and the relative efficacy and toxicity of anti-Parkinsonism drugs are compared. It is noted that the medical treatment of Parkinsonism is aimed at adjusting to normal the interaction between inhibitory dopaminergic and exitatory cholinergic systems at the level of the basal ganglia. A description of the use and therapeutic expectation of levodopa and levodopa combined with the dicarboxylase inhibitor, carbidopa, is presented. While their use is efficacious in improving brady kinesia, rigidity, postural stability and tremor, side-effects of psychiatric disturbance and involuntary movements result. The use of amantadine and the anticholinergic drugs as adjuvants of levodopa treatment are also described. Drugs which interact antagonistically when administered with levodopa are listed. Reserpine, phenothiazines, pyridoxine are noted as drugs which interfere with levodopa therapy. 7 references.

001888 Choquet, M.; Facy, F.; Davidson, F. no address **/Consumption of medication and risk of deviance among adolescents./** Consommation de medicaments et risque de deviance chez les adolescents. Bulletin de Medecine Legale, Urgence Medicale (Lyon). 20(4):374-389, 1977.

The significance of the use of psychotropic medication by adolescents is examined. Two groups of adolescents, a group of students during a school year and a group of adolescents hospitalized due to suicide attempts, were studied by means of two distinctive epidemiological surveys. An epidemiological approach to the former group revealed the existence of a deviant risk group characterized by poor adaptation to family and social settings, boredom and the use of psychotropic medication. An epidemiological study of the suicidal adolescents and a comparison between the normal and deviant groups confirmed these results and pointed to the risk of suicide by the use of such medication. It is suggested these results be used to implement preventive measures and to examine the real significance of the demands for psychotropic medication by adolescents. 8 references.

001889 Christensen, Dale Blaquiere. University of Minnesota **A study of physician drug prescribing adoption and discontinuation behaviors. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-18971 HC$15.00 MF$8.50 299 p.

Prescribing adoption and discontinuation practices for two new target drugs and one existing target drug were assessed among physicians in a prepaid group practice medical care

facility to identify and compare these practices and examine variables related to background, conditions of practice, sources of drug information used, and orientations and attitudes. Results confirmed the assumption that drug prescribing adoption patterns were similar across drugs and similar to diffusion patterns for other types of innovations. Drug prescribing discontinuation patterns were differed, and a linear function was noted in contrast to a cumulative normal frequency distribution for the two new drugs. Findings indicated that physicians drug prescribing characteristics varied according to the drug and physician specialty and generally challenge conventional views concerning the relative importance of physician variables in predicting time of first use of new drugs. (Journal abstract modified)

001890 Corbett, Lionel. Laboratory of Biological Psychiatry, Illinois State Psychiatric Institute, Chicago, IL **Depot neuroleptics in acute psychoses.** Current Psychiatric Therapies. 17:201-208, 1977.

The treatment of acute psychosis with antipsychotic agents administered as long-acting depot preparations, particularly the antischizophrenic drugs fluphenazine enanthate (FE) and fluphenazine deconate (FD), is described, and its advantages and disadvantages are discussed. Techniques and therapeutic expectations of FE or FD therapy are discussed. Side-effects such as striopallidal dystonia, autonomic and endocrine effects and postural dizziness, depression, and drowsiness are described. It is noted that no adverse drug interactions are known, however several precautions to the use of these depot drugs are listed. Three neuroleptic subgroups can be administered in depot form: phenothiazines, thioxanthenes and butyrophenones. 23 references.

001891 Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Some considerations on the biochemical basis of psychopharmacology. (Unpublished paper).** Washington, DC, NIMH, 1977. 23 p.

Neurochemical information essential to an understanding of the biochemical basis for psychopharmacological therapy is presented. Because the specificity of drug action is reliant on the tremendous complexity of a system composed of 50 billion neurons and only 20 identified neurotransmitters, the present task of psychopharmacology is to selectively maximize the therapeutic efficacy of psychiatric drugs by studying appropriate modifications that limit their side-effects. Antischizophrenic drugs have high affinity to binding with dopaminergic receptors and block the dopamine mediated stimulation of adenylate cyclase. On the otherhand, antidepressants appear to act on mechanisms that control serotonin or norepinephrine uptake. Whether this selectivity on the part of psychopharmacologic agents are an indication of specific disease etiologies has not yet been established. 74 references.

001892 Coutts, R. T.; Dawson, G. W. Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta T6G 2N8 Canada **Urinary excretion of phenolic metabolites of n-(n-propyl)amphetamine in man.** Research Communications in Chemical Pathology and Pharmacology. 17(2):349-352, 1977.

The urinary excretion of phenolic metabolites of N-(n-propyl)amphetamine in man was investigated, to identify previous failures to account for the total amounts of N-alkylated amphetamines administered to man. Two healthy male volunteers (ages 28 and 44) were each given oral doses of (+)-N-(n-propyl)amphetamine hydrochloride, and urine samples were collected for 24 hours. The samples from each volunteer were separately pooled and divided into three equal portions. Analytical results showed that in vivo metabolism of (+)-N-(n-propyl)amphetamine in man produced, among other products, two conjugated metabolites that were identified as 1-(4-hydroxyphenyl)-2-(n-propylamino)propane and 1-(4-hydroxy-3-methoxyphenyl)-2-n-propylamino)propane. In a 24 hour urine sample (pH uncontrolled), 13.4% of the N-alkylated amphetamine administered was excreted as the former metabolite, and 3.5% as the latter metabolite. Results are discussed in terms of the development of psychosis in chronic amphetamine abusers. 11 references. (Author abstract modified)

001893 Cowdry, Rex W.; Goodwin, Frederick K. Clinical Psychology Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Amine neurotransmitter studies and psychiatric illness: toward more meaningful diagnostic concepts. (Unpublished paper).** Bethesda, MD, NIMH, 1977. 42 p.

The state of the art in psychiatric diagnostic techniques with emphasis on biological measures of cognitive, emotional, appetitive, and autonomic functions is reviewed. Considerable progress is symbolized by the development of the Research Diagnostic System and similar systems with demonstrated reliability, but metabolite studies which provide a look into central neurotransmitter functioning are also of considerable value. Available data do not support the concept of a biological continuum with depression at one end, normality in the middle, and mania at the other end, although there is support for some significant clinical distinctions. Several techniques for extracting causal relationships from correlated metabolic observations are evaluated. It is suggested that although research has not as yet identified causal pathophysiological mechanisms in the major psychiatric disorders, the groundwork is being laid with the delineation of a complex set of interrelated biochemical mechanisms associated with disturbances of activity cognition and mood, and with the prediction of pharmacological activity and drug response. 58 references.

001894 Diaz, Jose Luis. Instituto de Investigaciones Biomedicas, Universidad Nacional Autonoma de Mexico, Mexico 20, D.F., Mexico **Ethnopharmacology of sacred psychoactive plants used by the Indians of Mexico.** Annual Review of Pharmacology and Toxicology. 17:647-675, 1977.

The ethnopharmacology of sacred psychoactive plants used by the Indians of Mexico is described and reviewed. Using an interdisciplinary approach, the history, botanical distribution and identification, ethnological uses, and psychopharmacology of these plants are discussed. The sacred plants are divided into six families which can be distinguished according to their effects: visionary, imagery inducing, trance inducing, deliriant, neurotoxic, and excitatory. An extensive table is included which summarizes the specific etymological, botanical, ethnological, pharmacological, and chemical information. 106 references.

001895 Douglas, Virginia. no address **How Canada holds down drug costs.** Forum. 1(2):2-5, 1977.

Canadian government programs to promote competitions among drug manufacturers through compulsory patient licensing, loans and grants to manufacturers, publishing of comparative price information, and laws enabling pharmacists to fill prescriptions from among all available brands, which have resulted in lower drug costs, are described. Results of a report on the Canadian experience by two Department of

Health, Education, and Welfare researchers, comparing data on 16 frequently prescribed drugs for Canada and the United States indicate that the average prices of the drugs fell 39.1% in Canada in comparison to a 2% drop in the United States. It is concluded that Canada's success in using a multifaceted approach to lower prices of a group of heavily prescribed drugs demonstrates the importance of competition in the drug inductry.

001896 Elmes, P. C. no address **The contribution of prescribed drugs to the incidence of accidental and deliberate poisoning in the community.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):517-521, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, an analysis of data submitted to the Belfast Division of the Poisons Service in Northern Ireland by doctors who treat Belfast's one and a quarter million people is presented. The increased incidence of drug and medicine overdose is demonstrated in both children and adults. It is noted that the accidental and deliberate prescribed drug poisonings are primarily the result of ingestion of medicines which are found in the home: barbiturates, other sleeping tablets, minor and major tranquilizers, tricyclic antidepressants, M.A.O. inhibitors, and oral contraceptives. Suggestions on reducing the availability of these drugs to potentially suicidal patients and their accessibility to children are offered.

001897 Fraser, H. F.; Kay, D. C.; Gorodetzky, C. W.; Yeh, S. Y.; Dewey, W. L. NIDA Addiction Research Center, P.O. Box 12390, Lexington, KY 40511 **Possible influence of opioid normetabolites (N) on opioid abstinence syndromes.** Pharmacologist. 19(2):157, 1977.

In a paper presented at the fall meeting of the American Society for Pharmacology and Experimental Therapeutics in Columbus, Ohio, August 1977, the possible influence of opioid normetabolites (N) on opioid abstinence syndromes was discussed. It is posited that depending on their pharmacologic activity and pharmacokinetic properties Ns formed via N-dealkylation of various opioids may influence the time course, severity, and nature of the observed abstinence syndrome including the source of abstinence points. Major portions of some opioids are converted to active Ns with a wide range of potencies and characteristics and which have longer half-lives and tendencies to accumulate on chronic administration than do the parent drugs. About 80% of acetylmethadol is converted to Ns which are active morphinelike agonists. This may be responsible for the delayed onset of acetylmethadol abstinence. The Ns of propoxyphene are weak morphinelike agonists which are extensively accumulated and may influence the nature and severity of propoxyphene abstinence. The Ns which have been studied appear to fully substitute for their chronically administered parent drugs, yet have a milder abstinence syndrome on abrupt withdrawal. It is suggested that Ns may be useful in opioid, including heroin, detoxification. (Author abstract modified)

001898 Giordano, Frank L. Dept. of Psychiatry, William Beaumont Army Medical Center, El Paso, TX 79920 **The benzodiazepines: pro or con.** Military Medicine. 142(8):629-631, 1977.

The usefulness and limitations of the benodiazepines are summarized and the combination of their pharmacologic properties and use patterns are considered in relation to benodiazepine abuse. Part of the popularity in prescribing these drugs lies in their safety as antianxiety agents. Except for potentiation of other CNS active drugs, there are few drug/drug interactions with the benzodiazepines. The muscle relaxant properties have encouraged their use in orthopedic problems as well as treatment of muscle spasticity. Much of the concern about overprescription seems rooted in the ethical system and related questions about how much anxiety is healthy. Street use and consequent addiction is similar to problems experienced with all sedative/hypnotic drugs. The problems of defining psychological dependence are considered and it is concluded that the utility of the benzodiazepines outweighs their abuse potential. 10 references.

001899 Giurgea, C.; Salama, M. Neuropharmacological Research Dept., UCB-Dipha, Brussels, Belgium **Nootropic drugs.** Progress in Neuro-Psychopharmacology. 1(3/4):235-247, 1977.

Nootropic drugs are proposed as a class of psychoactive drugs that selectively improve the efficiency of higher telencephalic integrative activities, and various features of nootropic drugs are presented under the headings of animal pharmacology, clinical pharmacology, and pharmacotherapeutics. The main features of the nootropic profile consist of: 1) enhancement of learning acquisition; 2) resistance to impairing agents; 3) facilitation of interhemispheric transfer of information; 4) enhanced resistance to brain aggressions; 5) increased tonic, cortical/subcortical control; and 6) absence of usual pharmacological effects of neuropsychotropic drugs. Piracetam is used as the prototype for nootropic drugs, and studies using piracetam in the treatment of chronic alcoholism and chronic brain syndrome due to aging are cited. Clinical/pharmacotherapeutic experiments are seen to corroborate findings of animal experiments that nootropic activity is based on a functional telencephalic selectivity. The basic mechanism of nootropics at the molecular and cellular levels are not yet known, although some recent data emphasized a possible role for cerebral ATP. 58 references. (Author abstract modified)

001900 Hemminki, Elina. Dept. of Public Health Sciences, University of Tampere, Vuolteenk. 11, SF-33100 Tampere 10, Finland **Polypharmacy among psychiatric patients.** Acta Psychiatrica Scandinavica (Kobenhavn). 56(5):347-356, 1977.

To determine the frequency of polypharmacy among psychiatric patients in Helsinki, and to ascertain whether this practice is supported by clinical trials, the drugs prescribed in 1 day to a sample of patients (n=694) in mental hospitals and outpatient clinics in Helsinki were studied. Results indicate that 69% of patients received more than one psychotropic drug in 1 day (61% received proper psychotropic drugs). On the average there were 2.1different psychotropic drugs per patient, and the maximum was six. A review of controlled clinical trials on the simultaneous use of more than one proper psychotropic drug in psychiatric diseases (excluding fixed combinations) revealed 14 trials. In only three trials was the combination better than its single components of placebo. Thus, there seems to be no evidence from clinical trials defending the frequent polypharmacy. A radical reduction in the number of psychotropic drugs prescribed for psychiatric patients is apparently desirable. 29 references. (Author abstract)

001901 Horn, Alan S.; Rodgers, John R. Department of Pharmacy, Laboratory for Pharmaceutical Chemistry, University of Groningen, The Netherlands **The enkephalins and opiates: structure-activity relations.** Journal of Pharmacy and Pharmacology (London). 29(5):257-265, 1977.

Following a literature review of known properties of the enkephalins, both the structural and conformational relations

between the opiates and enkephalins are analyzed. The X-ray structures of nine opiate drugs which exhibit a range of pharmacological activity were examined in detail leading to the theory that one of the reasons why the enkephalins and related peptides possess morphine like activity is because they have a tyrosine, hence a "tyramine" residue at the amino terminal position. It is emphasized that although the presence of the tyramine fragment may be of importance in explaining the action of several groups of agonists and antagonists, the stereospecificity/selectivity factor and the contribution of additional modes of binding from other portions of the molecule are also critical. This is evident from the reduction of activity on removing one or more residues from the C-terminal position of the enkephalins and also from the fact that drugs not possessing a tyramine moiety such as dextromoramide and methadone are active agonists at opiate receptors. 80 references.

001902 Inturrisi, Charles E.; Viederman, Milton; Rusk, Gary H.; Lowenthal, David T.; White, Robert P. Rogosin Kidney Center, New York Hospital-Cornell Medical Center, New York, NY **Combined seminar on the use of drugs in renal failure.** American Journal of Medicine. 62(4):527-554, 1977.

A series of papers are presented on the use of the following drugs in renal failure: narcotics, psychotherapeutic agents, antiarrhythmics, antihypertensives, sorbents, vitamin D and its analogues, anabolic hormones and nutritional supplements. The use of drugs in the treatment of patients with renal failure requires a knowledge of excretion, biotransformation and pharmacologic activity of metabolites. Indications and dosages of these drugs must be modified for patients with renal failure, and mechanisms of their biotransformation must be studied. This combined seminar presents the participants' studies and analyses of the problems surrounding the use of these various pharmacologic agents. 163 references. (Author abstract modified)

001903 Itil, Turan M.; Reisberg, Barry. Division of Biological Psychiatry, New York Medical College, Tarrytown, NY **Transcultural aspects of psychopharmacology.** Current Psychiatric Therapies. 17:325-332, 1977.

Transcultural psychopharmacology, the study of differences among cultural, ethnic or national groups in the basic mechanisms of and side effects to psychotropic drugs, is discussed. Studies of differences of biological and clinical aspects of pharmacological effects across sociocultural, environmental, and genetic variables are reported. The results indicate that ethnic and genetic factors play important roles in determining effects of drugs, but they are not interpretable according to national boundaries or geographic areas. The results of a survey concerning the use of psychotropic medication for 19 categories of severe psychiatric disorder in 52 countries are reported. 28 references.

001904 Jarvik, Murray E. no address **Psychopharmacology in the practice of medicine.** New York, Appleton-Century-Crofts, 1977. 516 p. $20.50.

A broad view of psychopharmacology, what it is concerned with, what its experimental techniques are, and what impact psychopharmaceutical knowledge has made on clinical problems is presented in 35 minireviews grouped into four major sections. Experimental use, psychotherapeutic use, and social uses of drugs are each given a section. Comprehensive references are included.

001905 Kanowski, S. Abt. fur Gerontopsychiatrie der Freien Universitat Berlin, Reichsstr. 15, D-1000 Berlin 19, Germany **Senescent brain: current status and implication in neuropsychopharmacology.** Progress in Neuro-Psychopharmacology. 1(3/4):249-256, 1977.

A critical review is presented of the facts and theories of senescent brain and of the main biological changes in aging brain and possible therapeutic effects of psychotropic drugs. It is noted that studies are lacking on the morphological, biochemical, and neurophysiological changes in senescent brain, and that systematic basic research is required for the understanding of the nature of the aging process in the central nervous system. Other topics include the increasing activity of monoamine oxidase in aging, protein metabolism in the brain, evoked potentials, and age related decline in cerebral blood flow. Psychopharmacological treatment of mental disorders and minor maladjustments in old age is seen to consist only of symptomatic therapeutics. Controlled clinical pharmacological studies are urged to assess the current psychopharmacological therapeutics and develop new drugs with gerotherapeutic and geroprophylactic effects. 41 references. (Author abstract modified)

001906 Keeler, Martin H.; Miller, William C. Dept. of Psychiatry, Medical University of South Carolina, 80 Barre St., Charleston, SC 29401 **Selection among benzodiazepines for alcohol withdrawal.** Southern Medical Journal. 70(8):970-973, 1977.

The benzodiazepines are discussed with regard to their use in managing alcohol withdrawal, and the advantages of using benzodiazepines for alcohol withdrawal are reviewed. Four pharmacologic differences among the benzodiazepines guide selection of the appropriate one: chlordiazepoxide, diazepam, oxazepam, or chlorazepate. Bases for selection include: 1) availability of other than oral dosage forms; 2) differences in additive effect with alcohol in producing central nervous system depression; 3) differences in anticonvulsant effect; and 4) differences in duration of effect in the body (i.e. half-life). Decreasing dosage schedules are preferred to a steady dosage. Illustrative dosage schedules for using chlordiazepoxide and diazepam to conduct alcohol withdrawal are given. 12 references. (Author abstract modified)

001907 Kline, Nathan S. no address **How I practice medicine.** Practical Psychology for Physicians. 4(11):26-29, 32-33, 1977.

A unique office procedure which enables a physician to see 700 new psychiatric patients a year is described by a pioneer in the use of psychotropic drugs. Before their first visit, new patients complete a computer analyzed history form. First, a psychiatric nurse conducts routine clinical tests and interviews the patient. A second consultation is conducted by an associate psychiatrist who reviews the patient's history forms, the nurse's notes, takes a psychosocial history of the patient, and makes a tentative diagnosis and treatment plan. Finally, the nurse, associate psychiatrist, and psychiatrist discuss the patient, diagnosis and treatment prior to the psychiatrist's interview with the patient. The clinic concentrates on resistent cases and emphasizes treatment with psychotropic drugs. The patient is examined by a staff internist and any cautions or contraindications to specific psychotropic drug therapy is reported. Administration of various psychotropic drugs and followup procedures are discussed.

001908 Lasagna, Louis. Department of Pharmacology and Toxicology, University of Rochester, School of Medicine and Dentistry, Rochester, NY 14642 **Prisoner subjects and drug testing.** Federation Proceedings. 36(10):2349-2351, 1977.

Ethical considerations involving the use of prisoners as subjects in drug research are discussed with particular emphasis on the impact of the recommendations of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research on pharmacological research. Objections to prison research are based more often on opposition to the evils of prison life than to unethical practices and to the memories of atrocities committed in the name of science in Nazi prison camps during World War II. The National Commission's pronouncements on prison research specifically illustrate this general phenomenon. Having decided that research on prisoners can be performed ethically, and having learned that most prisoner volunteers bitterly resent being deprived of the opportunity to participate in research, the Commission has nevertheless stipulated prison conditions that cannot realistically be met and thus has de facto eliminated such research. The most serious potential loss is the elimination of the unique facility in Lexington, Kentucky -- the Addiction Research Center. Predicting the addiction liability of drugs is not likely to be feasible in any nonprison setting, so that the addiction potential of new marketed drugs will be established in the future as it was in the past -- by trial-and-error in patients, who will become the unwilling, uninformed research subjects in this area. 4 references. (Author abstract modified)

001909 Lewis, James A.; Lewis, Barbara S. 4200 East 9th Ave., Container B150, Denver, CO 80262 **Deanol in minimal brain dysfunction.** Diseases of the Nervous System. 38(12, Section 2):21-24, 1977.

The use of deanol in that group of children characterized by restlessness, overactivity, and distractibility, and variously labeled minimal brain dysfunction (MBD), childhood hyperactivity, the hyperkinetic syndrome, or childhood learning disorders, is reviewed. EEG patterns of hyperactive children are discussed. The heterogenous nature of MBD makes patient identification important. The correlation between response to stimulants and various measures of brain function, suggests that at least two groups of patients should be studied: 1) those with physiological evidence of low arousal; and 2) those with evidence of normal or high arousal. Deanol could conceivably work best in those children least responsive to stimulants. 14 references.

001910 Maickel, Roger P. Section on Pharmacology, Medical Sciences Program, Indiana University School of Medicine, Bloomington, IN 47401 **Thanatopharmacology in the medical school curriculum.** Archives of the Foundation of Thanatology. 6(3):8, 1977.

The absence of thanatology and the unique problems posed by the use of drugs in treating the dying patient and the bereaved is noted in the traditional medical school curriculum. Traditional exposure of medical students to sympatholytic agents, sedatives, cholinergic blocking agents, and opiates is described. The development of tolerance to analgesics in the terminally ill and the uniqueness of atypical behavior induced by bereavement are discussed. It is suggested that the inclusion of thanatopharmacology would help to complete the education of future physicians.

001911 Manos, N.; Taratsidis, I.; Pappas, K.; Routsonis, C. Dept. of Psychiatry, Aristotelian University of Thessaloniki, Stavroupolis, Thessaloniki, Greece **Maintenance antipsychotic pharmacotherapy, relapse, and length of stay out of the hospital in chronic schizophrenics in Greece.** Journal of Nervous and Mental Disease. 165(5):361-363, 1977.

The relationship between maintenance antipsychotic pharmacotherapy, relapse, and rehospitalization of chronic schizophrenics in Greece was investiged. A retrospective study of 820 rehospitalizations of chronic schizophrenics showed no significant difference in the discharge/rehospitalization, discharge/relapse, and relapse/rehospitalization time intervals, between the patients who continued to receive their medication after discharge regularly, and the patients who discontinued their medication upon discharge. However, there seemed to be an increased social adaptability or tolerance of the psychotic behavior of the patients who had discontinued their medication, suggested by their longer relapse/rehospitalization time interval. 23 references. (Author abstract modified)

001912 Mapes, Roy E. A. Medical Sociology Research Ctr., Univ. College of Swansea, Park Bldgs., Park St., Swansea SA1 3DJ, Wales **Physicians' drug innovation and relinquishment.** Social Science & Medicine (Oxford). 11(11-13):619-623, 1977.

The processes involved in the selection of prescription drugs by general practitioners are analyzed, focusing on drug innovation and drug relinquishment. Drug innovation is considered an irrational process under certain systems of drug administration since general practitioners do not have sufficient knowledge to innovate with expectations of safety and effectiveness. Drug relinquishment, whereby a physician responds to the advocacy of professionals by ceasing to use a drug against which they have warned, is discussed in terms of the prescribing of nonbarbiturate hypnotics. It is noted that use of such drugs is still widespread in England, which may indicate that doctors with a pastoral orientation have a slight understanding of pharmacologically based therapy. Implications of the two processes are discussed, especially as regards physician autonomy. 32 references. (Author abstract modified)

001913 May, Franklin E.; Stewart, Ronald B.; Cluff, Leighton E. University of Florida, Gainesville, FL 32610 **Drug interactions and multiple drug administration.** Clinical Pharmacology and Therapeutics. 22(3):322-328, 1977.

Effects of multiple drug administration on adverse drug reactions were studied in 10,518 patients hospitalized on a general medical service during a 5 year period. Nine index drug groups, including analgesic, antacid, antiarrhythmic, antimicrobic, anticoagulant, antihypertensive, anti-inflammatory, diuretic, and sedative tranquilizer drugs, were selected for study. The average number of adverse drug reactions for the anticoagulant and antihypertensive drug groups was higher than for all other drug groups when classified by the number of drugs being taken concurrently. The rate of reaction for anticoagulant and antihypertensive drug groups was higher than the rate for other drug groups studied. These data suggest a higher risk of adverse drug reactions for patients receiving multiple drugs which may be the result from drug interactions. 7 references. (Journal abstract modified)

001914 McKearney, James W. Worcester Foundation for Experimental Biology, 222 Maple Avenue, Shrewsbury, MA 01545 **Asking questions about behavior.** Perspectives in Biology and Medicine. 21(1):109-119, 1977.

The paradox of seeking relatively simple therapies for complex social and personal behavior problems is examined from the perspective of the inapplicability of the cause and effect relationship, discrepancy between symptoms and their functional significance, and the tendency to construct concepts that may or may not be concretely related to what they

describe. The limits of cause and effect relations in behavior are proscribed by the notion that behavior is characterized by being arrived at in many different, and not self-sufficient ways. The error of equating function with behavior is demonstrated similarly, in the inherent differentiation of members of a behavioral group, e.g. alcoholics, or hyperkinetics. Thus, assigning structural properties to processes or relations is concluded to be self-defeating in that linguistic concepts per se cannot be taken as reality. It is suggested that refinement in the ways of conceptualizing human behavior is needed to avoid assigning structural properties to complex entities such as processes and relations. 20 references.

001915 no author. no address **Now RCA attacks memory-aid drugs.** Health and Social Service Journal (London). 87(4567):1581, 1977.

The controversy over plans to use residents of old age homes in England to test Piracetam, a new memory improving drug, is discussed. The Residential Care Association (RCA) condemned the proposal because the experiment will cause anxiety to the people in the homes. Supporters of the plan claim that only one or two people from each home would be involved in the small project.

001916 no author. no address **Involuntary administration of psychotropic drugs -- grounds for suit. Souder v. McGuire, 423 F.Supp. 830, (Pennsylvania). M.D. District Court. December 9, 1976.** Mental Health Court Digest. 21(4):3, 1977.

Affirmation of a suit by a former inmate at a state hospital for the criminally insane who had been subjected to unconsented medication, charging that he and others had been forcibly treated with psychotropic drugs in violation of their constitutional rights, is summarized. U.S. District Court upheld the action, noting that involuntary administration of drugs which have a painful or frightening effect can amount to cruel and unusual punishment, and that such medication amounts to an unwarranted governmental intrusion into the patient's thought processes in violation of the constitutional right to privacy.

001917 no author. no address **/Guidelines to reduce misuse of drugs./** Security. Nursing Mirror (Surrey). 154(19):xi, 1977.

A memorandum from the British Department of Health and Social Security on amendments to the Misuse of Drug Regulations 1973 is presented. It is indicated that the memorandum should be drawn to the attention of all staff responsible for the storage and/or administration of controlled drugs and particularly to those nursing officers with responsibility for midwifery and primary care services. Health Boards are asked subject to the availability of resources to review existing arrangements for the security of controlled drugs liable for misuse in hospital pharmacies, in health centers, isolated day clinics, and small hospitals without pharmacies and in hospital wards and departments, and to consider whether there is a local need to apply similar precautions to any other drugs which may be liable to misuse.

001918 Oettinger, Leon, Jr. University of California, Los Angeles, CA **Pediatric psychopharmacology: a review with special reference to deanol.** Diseases of the Nervous System. 38(12, Section 2):25-31, 1977.

General problems and issues in the field of pediatric psychopharmacology are outlined, and the use of deanol in the treatment of minimal brain dysfunction (MBD) is reviewed. The use of stimulant drugs with hyperactive children is defended, and pharmacotherapy is seen as the keystone to effective therapeutics. The MBD syndrome has multiple etiologies and varying symptomologies, but the demonstrable homogeneity is sufficient to retain the classification until separate groups can be defined. Drug therapy is considered practical and successful in adolescents and adults as well as in younger children and deanol is believed to be an interesting and probably effective drug for MDB. Standard procedures in drug development and screening are criticized. 81 references.

001919 Omatsuhara, Kosuke. Saieki Township Hospital, Saieki, Japan **On pharmacotherapy for the aged.** Psychiatria et Neurologia Japonica (Tokyo). 79(4):217-218, 1977.

At the 24th San'in District Symposium for Neuropsychiatrists, December 1976, Tottori, Japan, the results of a pharmacotherapeutic survey for common problems encountered in aged mental patients were analyzed. The pharmacotherapy in question was for brain arteriosclerosis related problems (especially depression), senile neurosis (with delusions and hallucinations), neurosis, and senility. It was found that about the same type of drugs was being prescribed to the elderly as to younger patients. More careful considerations were taken, however, with regard to possible harmful side-effects, and dosages were usually lower. In many cases, increasingly smaller dosages of drugs were used, and with those drugs which produced strong organic functional disabilities, they were usually administered with drugs to increase brain metabolism and circulation and with vitamins. It was concluded that this whole picture approach was the best method in administering pharmacotherapy to aged mental patients.

001920 Ortiz de Aleman, M. Yolanda; Castanon de Martinez, Victoria. Departamento de Higiene Mental, Hospital Infantil, Mexico D.F., Mexico **/Evaluation of different treatments in minimal cerebral damage./** Valoracion de diferentes tratamientos en el dano cerebral minimo. Neurologia-Neurocirugia-Psiquiatria (Mexico). 18(1):39-51, 1977.

A comparative study was carried out among 78 children aged 5 to 13 with learning and behavioral problems, in order to evaluate 3 different treatments: carbamazepine alone, carbamazepine plus psychotherapy and psychotherapy alone. The improvement among children who were treated with carbamazepine alone or with psychotherapy, was greater than that of those treated with psychotherapy alone. Carbamazepine was well tolerated and the study showed that it is used in the treatment of behavioral and learning disorders in children with minimal brain dysfunction. (Journal abstract modified)

001921 Pagan, J. no address **/Treatment of patients with delayed neuroleptics./** Sur la prise en charge des patients traites par des neuroleptiques-retard. Praktische Psychiatrie (Zurich). 56(4):104-106, 1977.

The use of long-acting neuroleptics, marking a fundamental development in the use of psychotropic agents and its history, are reviewed. At least 20% of patients had been neglecting to take their oral neuroleptics, despite strict physiological control. Intramuscular injection of long-acting drugs resulted in retarded absorption and metabolism of the drug over a relatively long period of time. The experimentation leading to determination of the i.m. route of administration is described. Advantages of the depot dosage are reviewed: the therapist is sure that the patient has received the medication, the therapist is certain of the dosage received by the patient, and the cheating of the patient in relation to not taking the necessary medication, which may lead to a defiant attitude toward the therapist, is resolved.

001922 Pagan, Juan. Hopital Psychiatrique, CH-1633 Marsens/Fribourg, Switzerland **/Problems engendered by administration of long-action neuroleptics./** Sur la prise en charge des patients traites par des neuroleptiques-retard. Praktische Psychiatrie (Zurich). 56(5):133-136, 1977.

Problems that may be engendered by administration of long-acting neuroleptics to mental patients are discussed. Following a brief listing of various retard medications two relatively specific complications are discussed: asthenic episodes, occasionally with an anxiety background, accompanied by somnolence of 2 or 3 days' duration following injection, and more particularly, depressive status. Some patients may view injection of a long-acting neuroleptic as an act of sadomasochistic aggression, whereas patients on oral dosage, for example, may feel as though they are no longer being treated for their illness because they no longer receive their daily pill. It is suggested that use of retard neuroleptics may affect the physician-patient relationship because the therapeist no longer need have daily contact with the patient and is somewhat remote. In conclusion the question is asked whether the use of long-acting neuroleptics truly represents progress in psychiatric care.

001923 Pearson, R. M.; Nestor, P. Clinical Pharmacology Unit, Royal Northern Hospital, London, England **Drug interactions.** Nursing Mirror (Surrey). 145(19):i-ii, iv-vi, 1977.

A study of drug interactions involving oral anticoagulants, hypoglycemic agents, digoxin, cytotoxic drugs and monoamine oxidase inhibitors is presented. It is indicated that these drugs have a low therapeutic ratio and an exaggerated response may be fatal. Untoward interactions involving certain antihypertensive drugs and anticonvulsants can also be important. The sites of drug interaction, alterations in the drugs outside the body and alteration of handling of drugs in the body are discussed and charts presented. It is suggested that a nurse should encourage the prescribing of the smallest number of necessary drugs, thus reducing the frequency of unwanted drug interactions.

001924 Plevova, Jarmila. Department of Pharmacology, Medical Faculty of Hygiene, Charles University, Prague, Czechoslovakia **System approach in experimental psychopharmacology and memory.** Studia Psychologica (Bratislava). 19(3):261-262, 1977.

Anokhin's formulation of a universal schema of the functional system as a dynamic organization of processes oriented to the organism's adaptation to its environment is discussed. Emphasis is placed on the contribution of the Valdman school of psychopharmacology to the study of adpative processes of the organism, including memory. It is suggested that an advance in experimental psychopharmacology is handicapped mainly by the slow development in the neurophysiology of emotions. Some processes evaluated as being closely connected with memory are how a drug affects the level of basic biological motivation, the level of emotional state, the level of understanding the significance of the trigger stimulus, and the level of the outcome of activity. 12 references.

001925 Prichard, B. N. C. University College Hospital, London, England **Beta-adrenoceptor blocking drugs.** Practitioner (London). 219(1312):501-508, 1977.

The pharmacology and uses of beta-adrenoceptor blocking drugs are discussed. Many applications of the drugs which were not originally predicted, including use in the treatment of arrhythmias, pheochromocytoma, hypertension, congenital heart disease, and dissecting aneurysm, have been discovered. Beta-adrenergic blocking drugs remain to be fully evaluated in some indications but are well established as valuable agents in a number of common conditions. Other than the cautious use of cardioselective agents in asthmatic disease, there is no conclusive evidence that there is any difference in the efficacy of the various beta-adrenergic blocking drugs in their various indications. 7 references.

001926 Puckett, Thomas T. Oklahoma State Bureau of Investigation, 12 SE 7th St, Lawton, OK 73501 **Psychopharmacologic agents in polygraph testing.** Polygraph. 6(2):149-156, 1977.

A brief review of psychopharmacologic agents and their possible effects on the reliability of polygraphic testing of subjects using them is presented. Listings of the major psychoactive drugs, by generic and trade names, are presented together with a summary of their therapeutic usage, effects and implications for polygraphy. These include: 1) hallucinogenic drugs and alcohol; 2) anxiolytic drugs (minor tranquilizers); 3) antipsychotic drugs (major tranquilizers); 4) antidepressant drugs; and 5) sedative, hypnotic, and psychogenic drugs. While empirical evidence on the effects of drug usage in real polygraphic situations is scarce, drugs which are specifically prescribed for their CNS effects logically may be expected to influence psychophysiological responses. Consequently the polygrapher should ascertain if a drug is being used when possible, perform a drug-free test when permitted by the subject's physician, and use caution and discretion in interpreting polygraph results when drug use is established or suspected. 6 references.

001927 Rickels, Karl; Hesbacher, Peter. 203 Piersol Building, University Hospital, 3600 Spruce Street, Philadelphia, PA 19104 **Psychopharmacologic agents: prescription patterns of nonpsychiatrists.** Psychosomatics. 18(5):37-40, 1977.

The relationship between the psychiatric diagnosis the family physician assigns and the type of psychotropic drug he prescribes was assessed using a 1970 survey of emotional illness and psychotropic drug use in 1190 patients from seven family practices from which 172 patients diagnosed with current emotional problems were sampled. Diagnosis was shown to be significantly related to the type of medication that was prescribed. The pattern of prescribing psychotropic drugs reflected rational and appropriate drug usage in which almost all anxious patients received the established pharmacologic treatment, antianxiety agents. Appropriate diagnosis was indicated in a subsample of 84 patients who also had a clinical evaluation by a research psychiatrist during the same office visit to their family physician. It is suggested by the data that rational and appropriate psychotropic drug prescription can be achieved by interested family physicians, and that the prescribing pattern of the physicians is not unduly influenced by pharmaceutical industry promotion. 10 references.

001928 Schuberth, J.; Ceder, G. Psychiatric Research Center, University of Uppsala, Uppsala, Sweden **Pharmacological, biochemical and clinical effects of 2-dimethylaminoethanol (Deanol): a critical reveiw.** Acta Pharmacologica et Toxicologica (Copenhagen). 41(Supplement 4):16, 1977.

At the 31st meeting of the Scandinavian Pharmacological Society, Umea, Sweden, August 15-17, 1977, the pharmacological, biochemical, and clinical effects of 2-methylaminoethanol (DMAE) were reviewed. Experiments that either support or dispute the proposal that DMAE has central stimulant effects are discussed. The possibility that DMAE is a possible precursor of brain choline and acetylcholine is discussed in terms of

several biochemical studies. It was suggested that the DMAE effects on choline metabolism are due to an enhanced base exchange reaction between DMAE and choline in phospholipids. The efficacy of DMAE in hyperkinetic children, and relief of the motor symptoms in patients suffering from tardive dyskinesia induced by neuroleptics or from Huntington's chorea are mentioned. It was concluded that the clinical results are in agreement with the concept of a central cholinomimetic effect of DMAE in patients with motor disturbances associated with a cholinergic hypofunction.

001929 Seiden, Lewis S.; Dykstra, Linda A. no address **Psychopharmacology: a biochemical and behavioral approach.** New York, Van Nostrand Reinhold, 1977. 451 p. $19.95.

A comprehensive review of the experimental literature on neuropharmacology, behavioral pharmacology, and clinical psychopharmacology is presented, intended for use of students and professionals in psychology, pharmacology, psychiatry, and the general biological and medical sciences. The studies are derived from basic biochemical, behavioral, and neuropharmacologic data obtained from animal studies of psychomotor stimulants, antidepressants, antianxiety agents, antipsychotics, analgesics, and hallucinogens. The first section covers behavior methods for assessing drug action, and pharmacologic and biochemical methods in psychopharmacology. The second section is devoted to the pharmacologic and biochemical basis of psychopharmacology. The third section covers drug behavior interaction. The section on pharmacologic and biochemical basis of psychopharmacology includes a review of the autonomic nervous system, serotonin and behavior, interactions between psychoactive drugs, catecholamines, and serotonin, and the pharmacologic and biochemical aspects of learning and memory.

001930 Shapiro, Arthur K.; Morris, Louis A. The Mount Sinai School of Medicine, New York, NY **Placebos in psychiatric therapy.** Current Psychiatric Therapies. 17:157-163, 1977.

A discussion of placebos in psychiatric therapy is presented, encompassing the significance of placebos historically, a definition of placebo and its therapeutic effects, a listing of correlates which affect the report and evaluation of the placebo effect, and a determination of the use of placebos in treatment of psychiatric symptoms. It is suggested that physicians should make themselves aware of placebo effects in order to enable themselves to better evaluate the effects of psychopharmacological therapy, contribute to the development of more flexible and appropriate procedures, and make therapy more comprehensive, resourceful and effective. 9 references.

001931 Shepherd, Michael. no address **Psychotropic drugs in psychiatry.** New York, Jason Aronson, 1977. 296 p. $15.00.

The impact of psychopharmacology on clinical psychiatry over the past 20 years is discussed. Three broad categories of enquiry are delineated: 1) psychotropic drugs, their classification, and basic clinical and pharmacological issues related to the use of specific medications; 2) therapeutic evaluation, the design of clinical experiments, and the interaction of nonpharmacodynamic factors with drugs in therapy; and 3) the wider social implications of psychotropic drugs for both the mentally ill and the general population. The impact of new compounds such as meprobamate, chlorpromazine, hydroxyzine, benactyzine, and reserpine is also analyzed.

001932 Smith, Mickey C.; Griffin, Lisa. Department of Health Care Administration, University of Mississippi, University, MS 38677 **Rationality of appeals used in the promotion of psychotropic drugs. A comparison of male and female models.** Social Science and Medicine (Oxford). 11(6/7):409-414, 1977.

To examine sex-role stereotyping in the promotion of psychotropic drugs, content analysis was performed on 329 different advertisements for psychotropic drugs which appeared in medical journals in 1974 classified by the nature of the sales appeal and the sex of the patient portrayed. Male patients were associated with the use of rational (as defined by the study) appeals significantly more often than were female patients. The illustration portions of the ads were associated with nonrational appeals in the majority of the ads, while the headline and text were more often associated with rational appeals. The influence of these advertising practices on prescribing has not been demonstrated, but the implications are important enough to warrant further study. 18 references. (Author abstract modified)

001933 Spohn, Herbert E. Menninger Foundation, Topeka, KS **Behavioral mechanisms of drug action in schizophrenia.** Final Report, NIMH Grant MH-20478, 1977. 11 p.

The effects of antipsychotic medication on psychological and psychophysiological dysfunction in chronic schizophrenics were investigated. Repeated testing of hospitalized chronic schizophrenics by means of a performance test battery, psychophysiological measurements, and clinical evaluation was performed. Drug treatment improved ability to maintain set, enhanced selective attention efficiency, increased perceptual judgment accuracy, and improved information processing efficiency. Results suggest that attentional functions in chronic schizophrenics are modified by antipsychotic drug treatment and the direction of such modification is toward normalization.

001934 Sprague, Robert L. Institute for Child Behavior and Development, University of Illinois, Champaign, IL **Psychopharmacotherapy in children.** In: McMillan, M., Child Psychiatry: Treatment and Research. New York, Brunner/Mazel, 1977. 332 p. (p. 130-149).

Three basic questions generated by the public controversy over drug treatment of children for behavioral problems are addressed as they relate to hyperactive and mentally retarded children. The issues are: 1) what is the prevalance of drug usage; 2) what are the effects of psychotropic drugs on the school performance of the child; and 3) what is the public impact of media claims and legal activities concerning extensive overuse of psychotropic medication with the mentally retarded. It is noted that 2% or 500,000 to 600,000 schoolchildren are currently receiving psychotropic medication, while 60% of the institutionalized mentally retarded children are receiving psychotropic drugs. It is contended that use of stimulant drugs on hyperactive and MBD children improves social behavior and, at low doses, enhances learning performance. However, neuroleptic medication for the institutionalized retarded reduces bizarre and stereotyped behavior but suppresses learning performance. It is contended that the controversy and publicity have had an impact. FDA's response and pending changes in regulations are discussed. It is felt that the lawsuits underway will force rapid upgrading of the standards for psychopharmacotherapy. Suggestions for the medical practitioner for averting the necessity for implementation of additional standards are offered. 41 references.

001935 Stafford, John R.; Fann, William E. Department of Psychiatry, Baylor College of Medicine, Houston, TX **Deanol acetamidobenzoate (Deaner) in tardive dyskinesia.** Diseases of the Nervous System. 38(12, Section 2):3-6, 1977.

The use of deanol acetamidobenzoate (Deaner) in the treatment of tardive dyskinesia is reviewed, and a three phase study (S=29) employing videotape rating and quantitative accelerometry for the assessment of movement post deanol administration is reported. Clinical response was pronounced in seven patients, moderate in nine patients and slight in 13 others. Deanol did not produce the anticipated elevation in choline levels postulated to be one mechanism of its action. The failure of deanol to achieve this effect may most probably be attributed to interval after last dose, to inadequate level of deanol or to some alteration in choline metabolism in the presence of deanol. The etiology of tardive dyskinesia at biochemical and structural levels is complex. For some patients improvement has been dramatic and clearly associated with deanol. Others appear to exhibit minimal response which cannot be differentiated from placebo or environmental effects. 39 references. (Author abstract modified)

001936 Tominaga, Hajime; Kobayashi, Ryozo; Takamuro, Shoichiro. Supporo National Hospital, Hokkaido, Sapporo, Japan **Clinical study of antiparkinson drugs used together with psychotropic drugs.** Iryo (Tokyo). 31(4):352-361, 1977.

A survey was taken among 30 Japanese national hospitals on the combined administration of antiparkinson drugs with psychotropic drugs. The antiparkinson drugs which were mainly used were of the aminopropanol and the phenothiazine types. In most of the facilities only small amounts of antiparkinson drugs were administered in conjunction with the psychotropic drugs. The side-effects of the antiparkinson drugs were similar when administered with autonomic nervous system interceptors and with tricyclic antidepressants. It was found that there were cases where psychotic symptoms worsened when the antiparkinson medication was discontinued. It was thus inferred that in some cases the antiparkinson drugs contributed to the effects of the psychotropic drugs. Side-effects from the antiparkinson drugs mostly included urination disabilities. 23 references.

001937 Vale, J. A. Poisons Unit, Guy's Hospital, London, England **The epidemiology of acute poisoning.** Acta Pharmacologica et Toxicologica (Kobenhavn). 41(Supplement 2):443-458, 1977.

At the 7th International Conference of the European Association of Poison Control Centres, held in Oslo, Norway during June 1976, statistics on acute poisoning derived from data collected during 1972 to 1974 at 66 hospitals which now form the South East Thames Regional Health Authority Area in Great Britain are presented. A more detailed retrospective study of all overdose patients admitted to one of those hospitals is also reported. Number of patients, age, sex, time of admission, type of drug(s) ingested, and treatment outcome and mortality statistics are included. Results of an examination of the data indicate that parasuicidal patients were generally young and were admitted predominantly during summer months, on weekends and in the evening. There was a decrease in the number of patients ingesting sedatives and hypnotics, and an increase in those poisoned by analgesics, tranquilizers and antidepressants, with barbiturates being the drugs most often ingested; the overall mortality rate in the S.E. Thames Regional Health Authority Area was 0.69%.

001938 Webb, Stephen D.; Collette, John. University of Victoria, Victoria, British Columbia, Canada **Rural-urban differences in the use of stress-alleviative drugs.** American Journal of Sociology. 83(3):700-707, 1977.

The differential prevalence of psychological stress in rural and urban areas is studied. Although it has long been alleged that urban life is more stressful than that experienced in rural districts, the available evidence is far from consistent. This study, employing stress alleviative drug use as an operational index of stress, examines rates of prescriptions for such drugs across the rural urban continuum in New Zealand. The data, obtained from a nationwide survey of pharmacists, are contrary to much of the conventional wisdom regarding urban psychological stress. It is concluded that stress related disorders are much more prevalent among rural than urban residents. 10 references. (Author abstract)

001939 White, James H. Huntington Beach Intercommunity Hospital, Huntington Beach, CA **Psychotropic drugs in child and adolescent psychiatry.** Current Psychiatric Therapies. 17:71-80, 1977.

Drug therapy for childhood and adolescent psychiatric disorders is overviewed, stating that no psychotropic drug should be administered to a child without having identified a target symptom and selecting a drug to which this symptom is likely to respond. The drugs of choice for the treatment of enuresis, hyperactivity, sleep disorders, anxiety, childhood psychosis, depression, school refusal, and pathological aggression for children and adolescents are listed. Graduated dosage levels for 1 week of therapy with children 5 to 12 years are given for the drugs methylphenidate, imipramine, dextroamphetamine, thioridazine, imipramine hydrochloride, diazepam, chlorpromazine, and trifluoperazine. It is advised that the drug treatment be as brief as possible with the minimum effective dose level, and that drug treatment should in no way substitute for essential environmental changes and/or psychotherapy. 25 references.

001940 Zander, Thomas K. no address **Prolixin decanoate: big brother by injection?** Journal of Psychiatry and Law. 5(1):55-75, 1977.

The psychiatric research and legal doctrine concerning the psychotropic drug prolixin decanoate (fluphenazine) is examined. Prolixin is a unique drug because, once it is injected into a person, its effects last from 2 to 4 weeks. Some courts are now considering the circumstances under which this drug should be forced upon an involuntarily committed individual. It is concluded that because of the shortcomings of psychiatric research of prolixin, and the adverse effects of the drug, courts should consider prolixin to be an experimental treatment modality like psychosurgery when deciding whether it should be forcibly administered to an involuntarily committed individual. 28 references. (Author abstract)

001941 Zander, Thomas K. no address **Prolixin decanoate: a review of the research.** Mental Disability Law Reporter. 2(1):37-42, 1977.

A review of the clinical literature in the field of psychotropic medication with the phenothiazine, Prolixin decanoate, is presented. Some of the reasons why the present research into Prolixin is inadequate are set out along with a suggestion for the aims of further research. To date, research has been biased in favor of the psychiatric establishment and has ignored the possible correlation between Prolixin and suicidal depression. Moreover, it is asserted that long-term, adversive effects, such as tardive dyskinesia and sudden, unexpected and unexplained death, have not been adequately investigated. It is suggested the Prolixin be considered an experimental drug until adequate investigatory studies have been carried out.

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